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ACQUIRED IMMUNE DEFICIENCY SYNDROME RESEARCH FUNDING

HEARING

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

NINETY-NINTH CONGRESS

FIRST SESSION

SPECIAL HEARING

Department of Health and Human Services
Nondepartmental witnesses

Printed for the use of the Committee on Appropriations

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ACQUIRED IMMUNE DEFICIENCY SYNDROME [AIDS] RESEARCH FUNDING

THURSDAY, SEPTEMBER 26, 1985

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN,
SERVICES, EDUCATION AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 9:30 a.m., in room SD–138, Dirksen Senate Office Building, Hon. Lowell P. Weicker, Jr. (chairman) presiding.

Present: Senators Weicker, Stevens, and Burdick.

Also present: Senator D'Amato.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

STATEMENT OF JAMES MASON, ACTING ASSISTANT SECRETARY FOR HEALTH

ACCOMPANIED BY:

- DR. JAMES WYNGAARDEN, DIRECTOR, NATIONAL INSTITUTES OF HEALTH
- DR. DONALD R. HOPKINS, ACTING DIRECTOR, CENTERS FOR DISEASE CONTROL, AIDS EFFORTS
- DR. DONALD IAN MACDONALD, DIRECTOR, ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION
- DR. FRANK YOUNG, COMMISSIONER, FOOD AND DRUG ADMINISTRATION

OVERVIEW AND SOCIETAL IMPACT—PRESENT AND FUTURE

Senator WEICKER. The hearing will come to order.

Today the subcommittee will receive an update on the public health challenge of AIDS. We do so in an environment of national uncertainty, uncertainty over the precise nature of AIDS, its risks and the sufficiency of Government's response to this epidemic.

As with any serious problem that is compounded by lack of public knowledge, AIDS has provoked anger and concern among and between our citizens. There is no necessity for such nonsense. What is needed, as always, is steady hands on the wheel. That is the best contribution which laymen can make to science in this crisis.

For example, one groundless fear that I want to dispel at the outset is that there has been inadequate funding for AIDS research in public health efforts. This is absolutely false. Whatever has been requested by Government research scientists and the medical professionals has been provided and this will continue to be the case.

Since chairing the subcommittee, the following sums have been appropriated specifically for AIDS: $61 million in fiscal year 1984; $108 million in fiscal year 1985; and $129 million approved for fiscal year 1986, and those figures are exclusive of the Food and Drug Administration.

The resources of the Government of the United States, including the world's premier biomedical research entity, the National Institutes of Health, are and will continue to be marshaled with the complete and bipartisan support of the Congress and the administration.

At present, this subcommittee has approved $129 million in AIDS funding for the fiscal year beginning next week, the full amount requested. If this hearing and subsequent research developments indicate additional funding is needed, it will be speedily and surely provided. That is our guarantee to the Nation.

Indeed, if testimony today reveals any potential shortfall in funding, I will amend my own bill at markup next Tuesday. The greater fear, however, is generated by a lack of full understanding of the disease itself and its risks to our citizens.

Today's witnesses, public and private, are among the most knowledgeable and most closely involved anywhere. They will establish a clear record of the current state of knowledge about AIDS and the future course of our research efforts. We most certainly do not have all the answers, but neither do all the questions remain unanswered. Indeed, for perhaps the first time in the history of mankind, we have an epidemic that has been identified, isolated, cloned all in 4 short years.

With this remarkable knowledge in hand, we are now moving to test methods blocking the spread of AIDS and from there attacking the disease itself.

Today we do not have the cure for AIDS, but neither do we have the ignorance of our ancestors who cast lepers in the sea and mentally ill in the dungeons. As our society presses the attack on AIDS with vigor and resoluteness, those among us who suffer this disease deserve understanding and help. We in the United States are one people, and by fact or law, there will be no pariahs among us.

One last observation. I referred earlier to the money specifically appropriated to AIDS. This is exclusive of the billions of dollars that go each year to basic scientific research. It is that ongoing research which gives us the ability to protect and enhance life in the face of any threat or any opportunity. To use a football analogy, without basic research, the AIDS offense would have started on our own 1-yard line. Because much diverse knowledge was already in hand, we started on the 40. That is the lesson for future budgets and those who seek to cut moneys for biomedical research.

Our first panel this morning is comprised of the top medical professionals in Government who are charged with responding to AIDS. I am very pleased to welcome you here this morning, and I would ask Dr. James Mason, the Acting Secretary of Health, to introduce his colleagues and begin with a review of the disease AIDS and its impact on society.

PREPARED STATEMENTS

Before you proceed, Dr. Mason, we will insert all the statements of all the HHS witnesses in the record in their entirety.

[The statements follow:]

STATEMENT OF DR. JAMES MASON

I am pleased to have this opportunity today to discuss the Public Health Service's efforts in combating the epidemic of AIDS and to review our financial commitment to these efforts. In my brief remarks, I would like to review what we have learned about AIDS since 1981 and to outline how we have used this knowledge to act responsibly and rapidly and to plot future strategies. Four PHS agencies--the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA); the Centers for Disease Control (CDC); the Food and Drug Administration (FDA); and the National Institutes of Health (NIH)--have made significant contributions to our understanding of the disease. Accompanying me today are Dr. Donald I. Macdonald, Administrator of ADAMHA; Dr. Donald R. Hopkins, Acting Director of CDC; Dr. Frank E. Young, Commissioner of FDA; and Dr. James Wyngaarden, Director of NIH. In their testimony, each will describe the efforts under way and the agency's plans for both the request made in the FY 1986 budget as well as those made recently for supplemental funds.

I would like to mention that the activities of the agencies are coordinated through a PHS Executive Task Force on AIDS chaired by the Assistant Secretary for Health which meets biweekly. This Task Force was established by former Assistant Secretary for Health Edward Brandt, and it continues to be an important forum to communicate, coordinate, review policy, and to formulate future plans for combating this dread disease. Within this Task Force, subgroups are charged with working within specific areas. These include the following:

- Vaccine Development and Therapeutic Intervention: Chaired by Dr. James Wyngaarden, NIH.

- Epidemiology and Prevention: Chaired by Dr. Donald Hopkins, CDC.

- Blood and Blood Products: Chaired by Dr. Harry Meyer, FDA.
- Psychological, Psychiatric, and Addictive Aspects: Chaired by Dr. Donald Macdonald, ADAMHA.

Through these subgroups, the agencies coordinate their efforts in a number of areas, including blood donor studies and development of animal models. In testimony of the agency heads, you will hear of the role each agency plays in these activities. There are also three panels of the PHS Executive Task Force on AIDS which coordinate activities in information development, resources, and science.

Acquired immune deficiency syndrome is a disease of epidemic proportions and a national health problem unprecedented in recent history. There is little question that today we are witnessing an epidemic of fear. People from all walks of life feel threatened by AIDS, and they feel helpless in the face of an almost universally fatal disease. Secretary Margaret Heckler has made control of this disease our number one public health priority.

The first case of AIDS was reported to the Centers for Disease Control in June of 1981, although we now believe that the onset of the disease in the U.S. may go back to 1977. We do not know its origins. Some recent studies suggest that the disease existed in central Africa in the early to mid-1970s. The number of AIDS cases reported in the U.S. has doubled each year as shown in Chart 1. We know of over 13,000 reported cases, but we believe that as many as one-half million to one million persons in the United States are infected with the AIDS virus. Studies in homosexual men infected with the AIDS virus indicate that 5 to 10 percent will develop AIDS within two to five years after becoming infected. The case fatality rate among AIDS patients is high. Over 50 percent of reported cases are known to have died. For those diagnosed with AIDS for two years or longer, the mortality rate is over 85 percent.

There is no doubt that the principal mode of transmission is through sexual contact. Chart 2 shows that nearly 75 percent of the AIDS cases among adults are related to sexual transmission. Most of these cases (about 74 percent) have occurred among homosexual or bisexual males. Another 1.2 percent have occurred among heterosexual partners of high risk groups.

Another major mode of transmission is through sharing of needles among IV drug abusers. This mode accounts for from 17 to 25 percent of cases. There is some overlap between homosexual men who use IV drugs. The risk for transmission of the AIDS virus through transfusion of blood or blood products, which in the past accounted for 2.2 percent of AIDS cases, or through transfusion of clotting factor (0.8 percent of cases that occurred in persons with hemophilia) has been virtually eliminated. This is because a screening test, which detects antibody to the AIDS virus, is now used routinely by blood banks and plasma centers. In addition routine heat and chemical treatment render clotting factor free of the virus. In March 1983, the PHS issued guidelines recommending the voluntary avoidance of donation of blood and plasma by members of high-risk groups. Continued enforcement of these guidelines by centers provides an added layer of protection from acquiring AIDS through transfused blood, blood products, or clotting factor.

We now know that infected mothers can transmit the virus to their babies across the placenta and, likely, through breast milk. Although the AIDS virus has been isolated from human saliva and tears, there is no evidence that transmission has occurred through these routes.

There has not been a single case of AIDS reported to us in family members of AIDS patients, except for sexual partners and children born to infected women. In studies of over 300 household contacts, not one person--other than a sexual contact or a child born to an infected mother--has become seropositive or developed AIDS as a result of living with AIDS patients. In studies of more than 1,472 health care workers, who have close contact with very ill, often hospitalized, AIDS patients, not one has developed AIDS or become seropositive as a result of contact with patients, other than through needle stick injury. Eighteen health care workers have had positive test results. Of these 18, all but three belonged to risk groups. The other three suffered needle stick injuries, and we continue to strongly urge people handling needles to observe the precautions PHS published in November 1982.

These studies allow us to say with a high degree of certainty that the AIDS virus is not spread through casual contact. This would include sharing of meals, coughing, or sneezing. We have done our utmost to get this message across to the public and the press in the past few weeks as concern has mounted about school children with AIDS.

Chart 3 shows our progress to date in combating this disease. It has been remarkable. We know who is at risk and how the disease is transmitted. The weekly publication of the Centers for Disease Control, Morbidity and Mortality Report (MMWR), is one of our most rapid channels of communication to the Nation's public health community. The MMWR has carried our recommendations dealing with safety of the blood supply, personal behavior as a preventive measure, and use of the blood screening test. On August 20, we advised that in general, school-age children with AIDS should be allowed to attend school, while proposing a more restricted environment for younger children with the disease. These guidelines are provided to assist State and local decisionmakers. In addition to using the MMWR as a vehicle for communicating to the public health community, we have embarked upon a major plan for the prevention and control of AIDS which will be published shortly in Public Health Reports, the official journal of the PHS.

We understand the cause of AIDS. In 1984, a retrovirus, human T-lymphotropic virus, type III (HTLV-III)/lymphadenopathy associated virus, was identified as the cause of AIDS. It is unusual to have the cause of a disease identified so quickly, especially, as in the case of AIDS, where the discovery of a new agent was involved. In addition, scientists have made significant progress in describing the structure of the virus and understanding its effect in man.

Discovery of the AIDS virus allowed us to develop a test for use in blood banks and plasma centers to prevent transmission of the disease through transfusions of blood and blood products. The HTLV-III antibody test is now used to test every unit of blood or plasma in the United States. Heat and chemical treatments were developed to render clotting factor essentially free of AIDS virus, and as a result, hemophiliacs are provided an added layer of protection from acquiring the disease. Because of the long incubation period of AIDS, however, we will continue to hear of new cases in hemophiliacs and recipients of blood transfusions who were infected before the HTLV-III antibody and other preventive measures were available.

Regrettably, there is currently no effective treatment for those with AIDS. We have screened over 100 drugs and a number of them are in various stages of clinical testing. Some of the most promising drugs work by decreasing the spread of the virus in patients. You will hear from Dr. Wyngaarden and Dr. Young of their efforts to discover and bring to the market drugs of promise.

Vaccine development is under way, but our initial optimism at having a vaccine within a short time after the discovery of the HTLV-III virus has been stymied. THe HTLV-III antibody that forms the basis of the blood test is not the one that protects against the disease. The development of a vaccine will require additional basic research.

Neither a vaccine nor an effective treatment is on the immediate horizon. But we do know enough about the transmission of AIDS to substantially curtail the spread of the disease if current knowledge were applied. Choice of personal behavior is a powerful tool for control of AIDS.

Accordingly, we have accelerated our public information and education effort to advise Americans of the current information about transmissibility of the disease and the bahavioral preventive measures they can take. Many communities throughout the United States are already actively involved in programs aimed at prevention and control of AIDS; others need encouragement. We will continue to work closely with State and local health departments and other community groups. In addition, we are planning a major national information campaign.

Last week at a press briefing, we made the following recommendations. We will continue to promulgate these messages.

o Do not have sexual intercourse with AIDS patients, with members of the risk groups, or with people who are positive for the AIDS virus. But if you do, it would be prudent to use a condom and avoid sexual practices such as anal intercourse that may injure tissue.

o Do not use IV drugs. But if you do, do not share needles.

- Women who are sex partners of risk groups members or who use IV drugs should consider the risk to their babies before pregnancy.

In FY 1986, we have requested $126.3 million for our AIDS effort. I should note that $6.6 million of the total request is for FDA, whose budget is considered by the Appropriations Subcommittee on Agriculture and Related Agencies. The FY 1986 request includes a $40.7 million increase over the original FY 1986 President's Budget which was submitted to the Congress in February of this year (see Chart 4). The need to increase spending for AIDS was communicated by Secretary Heckler in a July 19 letter to the appropriations committees. This was followed up by a formal budget amendment on September 9, 1985. These resources will

- Significantly enhance our ability to implement a major preventive strategy through the initiation of Community Health Education/Risk Reduction programs throughout the Nation;

- Expand the NIH efforts towards identifying and testing antiviral compounds and developing a vaccine; and

- Expand necessary epidemiologic studies and surveillance activities.

The resources for AIDS have grown from a level of $5.5 million in FY 1982 to $126.3 million in FY 1986 (see Chart 5). The PHS resource level has grown each year as the Department has identified opportunities for expanding its efforts against this disease.

The PHS, through its Executive Task Force on AIDS, monitors continually plans versus accomplishments and solicits the identification of new avenues for accelerated progress in controlling this disease. Because of the dynamic nature of the PHS effort to conquer AIDS, this monitoring process permits us to explore and pursue every reasonable opportunity to bring this disease under control. The previously mentioned $40.7 million increase in spending resulted from a reassessment which was conducted during the spring of this year. Another reassessment of AIDS efforts was recently completed and, as a result, we believe there is a need to expand beyond our current request in order to evaluate new drugs and therapies and to gain a better understanding of the prevalence of AIDS.

This disease is the Department's number one public health priority. We will continue to reassess our efforts in order to make maximum progress in our fight against this disease. Within a short period of time, an analysis of funding alternatives and plans for these additional FY 1986 activities is expected to be completed.

Mr. Chairman, this completes my statement. I would be pleased to answer any questions you or other Subcommittee members might have.

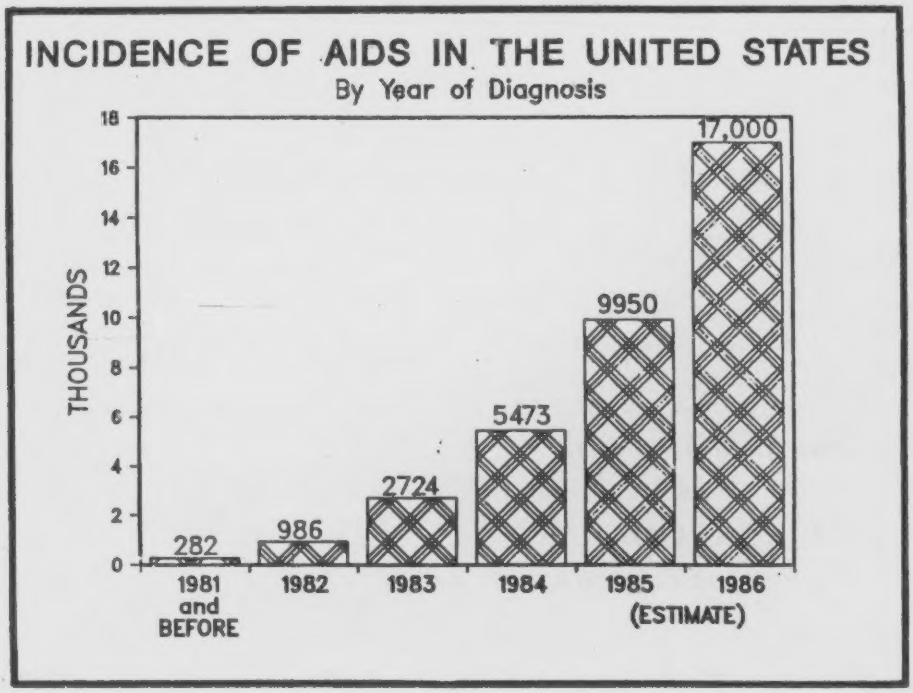

CHART 1

AIDS RISK GROUP PATTERNS

(Percentage of New Cases)

	1982	1985
HOMOSEXUAL OR BISEXUAL MEN	71.6	73.8
INTRAVENOUS (IV) DRUG ABUSERS	16.7	16.6
PERSONS WITH HEMOPHILIA	0.6	0.8
HETEROSEXUAL PARTNERS OF HIGH RISK GROUPS	1.0	1.2
RECIPIENTS OF BLOOD OR BLOOD PRODUCTS	0.8	2.2
OTHER *	9.3	5.5

* INCLUDES HAITIANS WHICH WERE CLASSIFIED SEPARATELY BEFORE 1984

CHART 2

AIDS PROGRESS

PROBLEMS	ACTION TAKEN
• UNDERSTANDING RISK GROUPS AND TRANSMISSION	• EPIDEMIOLOGY DESCRIBED
• UNDERSTANDING THE CAUSE	• VIRUS (HTLV-III) IDENTIFIED
• PROTECTION OF NATION'S BLOOD SUPPLY	• GUIDELINES FOR BLOOD BANKS • BLOOD TEST DEVELOPED & IN USE
• PROTECTING HEMOPHILIACS	• HEAT TREATMENT DEVELOPED
• TREATMENT THERAPIES	• SCREENING OF OVER 100 DRUGS • CLINICAL STUDIES OF PROMISING DRUGS UNDERWAY
• VACCINE DEVELOPMENT	• STUDIES UNDERWAY
• PREVENTION IN HIGH RISK GROUPS	• PUBLIC EDUCATION PROGRAMS • GUIDELINES DEVELOPED

CHART 3

AIDS
FY 1986 REQUEST
($ in millions)

	Original Request	Budget Amendment	Revised Request
ADAMHA	$ 2.9	$ 0.6	$ 3.5
CDC	18.7	26.9	45.6
FDA	3.7	2.9	6.6
NIH	60.3	10.3	70.6
TOTAL, PHS	$85.6	$40.7	$126.3

CHART 4

AIDS - FUNDING HISTORY
($ in millions)

	Fiscal Years				
	82 Actual	83 Actual	84 Actual	85 (Est.)	86 (Est.)
ADAMHA	--	$ 0.5	$ 2.8	$ 3.2	$ 3.5
CDC	2.0	6.2	13.8	33.2	45.6
FDA	0.1	0.3	0.8	9.0	6.6
NIH	3.4	21.7	44.1	63.5	70.6
TOTAL, PHS	$ 5.5	$28.7	$61.5	$108.9	$126.3

CHART 5

STATEMENT OF DR. JAMES WYNGAARDEN

I am pleased to provide the Committee with an overview of ongoing activities and research objectives of the National Institutes of Health (NIH) on Acquired Immunodeficiency Syndrome (AIDS). Although tremendous progress has been made, much remains to be learned concerning the treatment of AIDS patients and the ultimate prevention of this deadly disease.

AIDS continues to be recognized by Secretary Heckler as the number one public health priority of the Department of Health and Human Services (HHS). With the support and leadership of the Secretary, the Administration, and the Congress, NIH has maintained a strong and growing research effort prior to and since the first AIDS patients were admitted to the NIH Clinical Center more than four years ago. We are committed to determining the frequency and distribution of AIDS in the population, its mode of transmission, and the means for treatment and prevention of the disease.

Although the problem of AIDS is far from solved, research carried out by NIH grantees, and at the NIH itself during these years, has led to a dramatic accumulation of information about various aspects of the disease. Certainly, tremendous impetus for the AIDS research program was provided by the clear delineation by scientists in the National Cancer Institute (NCI) early in 1984, that a retrovirus, human T-cell lymphotrophic virus type III (HTLV-III), is the underlying cause of AIDS. This discovery led to changes in direction in many research studies, opened new opportunities for research on treatment of patients and on prevention strategies, presented new avenues for development of vaccines, and resulted in a blood screening test to reduce transmission through transfusion.

We recognize that AIDS research and its associated planning must be a dynamic process, punctuated by new discoveries and the inevitable adjustments that these developments impose. The NIH planning and budget processes allow the flexibility needed to redirect our focus and best utilize our resources. To assure that NIH would be prepared to respond rapidly and be fully informed of all AIDS activities, the NIH Working Group on AIDS was established in 1982 to coordinate and exchange information among the Bureaus, Institutes, and Divisions of NIH, as well as with the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), the Centers for Disease Control (CDC) and the Food and Drug Administration (FDA). This high level of collaboration was enhanced by the creation by the Assistant Secretary for Health of the PHS AIDS Executive Task Force to expedite the large-scale practical applications of AIDS and AIDS-related findings. The NIH working group was replaced by the NIH AIDS Executive Committee, which was established in June 1984. The purpose of the NIH AIDS Executive Committee is to keep the NIH Director fully informed on AIDS and AIDS-related matters. The committee also provides a mechanism to heighten coordination among elements of the NIH so that all new research opportunities are fully exploited. As the need arises, the NIH AIDS Executive Committee establishes subcommittees to address specific problems, such as the subcommittee for the development and testing of prophylactic and therapeutic modalities for the control of AIDS and the subcommittee for the development of appropriate animal models.

CURRENT DIRECTIONS

Research supported and conducted by NIH includes studies of the chemistry and biology of the causative virus itself; basic studies supporting the development of reliable diagnostic tests for AIDS; epidemiologic studies, including examination of cofactors that might play a role along with HTLV-III in causing AIDS; work aimed at reconstituting the immune system in AIDS patients; inhibiting and eradicating the retrovirus (HTLV-III) with antiviral agents and controlling the opportunistic infections and cancers characteristic of the disease; application of several techniques to the development of vaccines, including the search for animal models for AIDS; and studies aimed at more effective screening of donated blood.

Special emphasis is being given to drug research and testing in the treatment of AIDS. With the discovery of the causative agent, scientists now know that research on treatment modalities must be simultaneously focused on developing antiviral agents to inhibit the replication of the virus, reconstituting the immune system, and treating the opportunistic infections that afflict AIDS patients. It is likely that the patients will have to be treated with at least two agents simultaneously, an antiviral agent and an immune enhancer, in order to successfully combat the disease. However, more research is needed to answer this point definitively. Antiviral agents identified as having clinical potential are currently being tested or are in preparation for testing. Studies must first be done to ensure that these drugs are generally safe, and will not further compromise the weakened state of the patient with AIDS.

In regard to vaccine development, NIH researchers working in close cooperation with colleagues at the FDA are currently investigating a number of preparations made by breaking up the whole AIDS virus and extracting antigens. These preparations are now being tested in animals for evaluation of their effectiveness as a potential vaccine. Additionally, a number of NIH investigators are using recombinant DNA technology in an attempt to clone appropriate gene segments of HTLV-III.

RESEARCH OBJECTIVES

The NIH will capitalize on the extensive research on AIDS-related disorders, principally through epidemiologic studies to clarify the natural history of the disease and through additional work toward the development of vaccines and antiviral agents. Basic research will continue. Specific activities proposed for FY 1986 will include the following:

Basic Research

The rapid progress that has been made thus far in AIDS research is due in large part to the extensive and farsighted previous investments in basic science, particularly in the areas of immunology and virology. Of course there is still much to be learned about the virology and pathogenicity of the virus. Therefore, the Institutes will continue to actively support basic research involving antigenic viral components, stressing antigens that are common to many virus strains and would elicit neutralizing and/or protective antibodies; latency; incorporation of the viral genome in the host cell and activating factors; inhibition of viral growth; isolation of the virus from various body fluids; identification of markers for predicting occurrence of clinical disease in virus-exposed individuals; development of diagnostic tests and viral isolation; and the determination of genetic and other variations among HTLV-III isolates.

Epidemiologic Studies

A wide range of epidemiologic research on AIDS is being conducted at NIH, by its grantees and in collaboration with other agencies of the PHS. The objectives of these studies are to develop an understanding of how infection occurs, how frequently and under what circumstances HTLV-III infection persists in infected individuals, and which infected individuals are most likely to transmit HTLV-III; the severity of disease in relation to time and source of infection; risk factors; time frames for the development of antibodies to HTLV-III; and the role of host factors and cofactors in disease risk. Examples include:

- Studies in various populations to assess the prevalence of HTLV-III infection by using the HTLV-III antibody ELISA test and viral isolation. Groups to be examined include: Homosexual men, hemophiliacs, drug users, family contacts, hospital and laboratory personnel, blood donors, and several populations in the United States and in Haiti, Central Africa, and the Far East.

- The National Institute of Allergy and Infectious Diseases (NIAID) support of a large multi-center study of the natural history of AIDS in homosexual men. Specifically, 5,000 homosexual men in Baltimore, San Francisco, Chicago, Los Angeles, and Pittsburgh are being followed longitudinally for three years. The objective is to resolve issues concerning the clinical spectrum of HTLV-III infections, the implications of a positive serologic test for an individual, the prevalence of circulating and/or shed virus in antibody-positive persons, and the prognosis for seropositive individuals with mild or no signs of disease. A similar group of men from New York will be evaluated. While this study was originally set up to collect specimens in an attempt to determine the etiologic agent, it has been converted into a natural history study similar to the multicenter study. Biological specimens collected from each of these populations will be made available to intramural and extramural scientists for study.

- A large study of the natural history of HTLV-III infection in newborn children. This involves the identification of HTLV-III positive pregnant women, spouses of patients, parenteral drug users, and Haitians, and the subsequent laboratory and clinical evaluation of their offspring up to two years of age.

- Study and treatment of AIDS-associated ocular infections. Our investigators have demonstrated the presence of HTLV-III in human tears. Although it has not been shown that AIDS is transmissible through tears, this work points to the need to sterilize ophthalmic instruments that come in contact with the eye. Future work will examine the significance of HTLV-III in ocular fluids.

- A large study of AIDS in Zaire through cooperative efforts of the NIAID, CDC, the Zairian Ministry of Health, and the Belgian Institute for Tropical Medicine. Special attention is being paid to the role of heterosexual contact and transmission within family units.

- Followup studies of documented regional differences in the prevalence and exact nature of HTLV-III antibody in Kenya. The purpose is to clarify the basis for low AIDS case rates in areas endemic for HTLV-III.

- Expansion of projects related to the high rates of viral isolation in seronegative sexual contacts of high-risk group members.

- A study of HTLV-III transmission in seropositive, pregnant, drug-using females and their offspring, with followup of the children to monitor seroconversion, immune function, and risk of AIDS.

- Interviews of persons occupationally exposed to HTLV-III regarding known AIDS risk factors and details of exposures (particularly needle-stick injuries) and serial collection of blood samples.

- A followup of a drug-user cohort study which indicates striking geographic differences in seropositivity to assess changes in seroprevalence over time and the risk of AIDS and AIDS-related illnesses.

- Evaluation of immune function of individuals at high risk for AIDS for at least two years to determine whether any of them develop AIDS symptoms. Attempts will be made to identify immune abnormalities that may be predictive for AIDS and could help elucidate the mechanisms leading to disease.

- Studies to determine the role of agents as cofactors and their role in disease pathogenesis.

- A study with clinical centers in New York, San Francisco, Miami, Los Angeles, Detroit, and Seattle to determine the incidence and natural history of HTLV-III infection. The study will include 1,000 hemophiliacs, 100 persons with sickle-cell disease, and about 150 with Cooley's anemia. Family members, sexual partners, and persons with the same disease who are less frequently transfused will be among the control population in this study. The results of the study will be important to understanding the role and relative risk of various types of blood components in transmission of HTLV-III.

- Collection of serum samples from randomly selected volunteer blood donors at major blood centers in New York, San Francisco, Miami, and Los Angeles prior to the development of the HTLV-III test. This serum repository will be used for testing antibodies to HTLV-III, identification of seropositive donors and recipients of blood products from these donors, followup of the recipients, and data analysis.

  This project also involves the study of the natural history of alterations in immune system function in heavily transfused patients and the relation of these alterations to the clinical development of AIDS.

- Further studies related to AIDS encephalopathy and the substantial data that the retrovirus HTLV-III is present in the brain of AIDS patients. It is of clinical, therapeutic, and epidemiological importance to determine what percentage of currently seropositive individuals may harbor HTLV-III in their brains.

- Investigation of the role of protein components of saliva that serve as a natural defense mecnanism against Candida albicans, an opportunistic infection. There appears to be a definite association between AIDS and the presence of Candida albicans. The successful development of an assay for the antifungal proteins in saliva may help identify those at high risk of developing AIDS.

Treatment

The objective of studies related to treatment is the development and evaluation of antivirals and immune stimulants, as well as combinations of these which are effective against AIDS. Research objectives being pursued in close collaboration with FDA in this critical area will include:

- Immediate investigation of the efficacy and safety of HPA-23, made possible by the recent review of an investigational new drug (IND) application by the FDA.

- Determination of whether a proposed therapy is effective. One highly sensitive indicator of the effectiveness of systemic treatment of AIDS is the persistence or disappearance of the ocular signs associated with cytomegalovirus retinitis in the 30 to 40 percent of AIDS patients estimated to have this opportunistic eye infection.

- Methodologies for the control of opportunistic infections, such as evaluating the effectiveness of the antiviral drug 9-(1,3 dihydroxy-2-propoxymethyl) guanine (DHPG) in cytomegalovirus retinitis and colitis viral infections, often present in AIDS patients.

- Phase I studies (that is, human subject studies designed to establish tolerable toxicities and monitor for pharmacological effects over a range of doses) of antivirals and immune modulators, which are being done in our intramural programs. Some of these studies involve interleukin-2, Ribavirin, Foscarnet, and Suramin. Agents having a tolerable toxicity level at dosages that show some stimulation of the immune system or are active against the AIDS virus will then move on to Phase II studies. (Phase II studies are basically an extension of Phase I studies, involving larger numbers of patients, to determine the effective dosages.) If these studies are successful, controlled efficacy trials, Phase III studies, will follow.

Of the agents under review, Suramin continues to be viewed as a promising drug, as there is strong evidence that it has clinical activity against HTLV-III. To date, a number of patients are involved in trials with this drug, and more trials are planned with larger numbers of patients. NIH continues to support these trials, which are performed both intramurally and at a number of institutions receiving extramural support.

- Studies involving a large group of patients who are symptom-free high-risk subjects, subjects with AIDS-related complex (ARC), or subjects with AIDS. Investigators have defined the immunologic abnormalities in AIDS, and the plan is now to apply this information to the development of therapeutic approaches using immunorestorative agents.

- Use of bone marrow transplants in an attempt to restore the immune system. Such transplants have been performed in two pairs of identical twins. Experience with this study showed there was some improvement in immune function, although one patient subsequently died. However, at that time the causative agent had not been identified, and efforts were directed at restoration of the immune system alone. We now know that combined therapy is indicated, because unless the virus itself is blocked, the immune system will deteriorate in the same way as the initial immune system did. Currently, three pairs of identical twins are being studied. Suramin is being combined with bone marrow transplantation in the three patients with AIDS. It is too early to predict the results of these efforts.

- Clinical trials with Ribavirin in the treatment of pediatric AIDS. Additional agents which have been effective in the treatment of animal retrovirus infections will be tested in chimpanzee HTLV-III models and in the Rhesus monkey AIDS model. In Phase I, promising antiviral agents will be tested for their efficacy in eliminating viremia. Serum and cerebrospinal fluid (CSF) levels of virus will be evaluated against dosage and toxicity. The animal model further allows testing of drug efficacy in clearing brain infections (as shown by selective serial brain biopsies) and assessment of antiviral efficacy and toxicity in pregnant and newborn HTLV-III infected animals.

Prevention

NIH is working closely with agencies throughout the PHS in developing improved methods for detection and control of this disease. The principal objective of NIH efforts in the prevention area is to develop and evaluate better approaches for detecting infection as well as to develop passive and active immuno-prophylaxis. Broad-scale prevention and control activities emphasizing educational and information exchange must begin, in the absence of a vaccine and specific therapy. They should be based on current best public health judgment. A variety of activities will be undertaken in the prevention area including:

- Improved methodology to detect AIDS antibody.
- Attempts to develop methodologies for early detection of disease.
- Simple, rapid, and sensitive methods for the detection and isolation of HTLV-III.
- A great many methods of vaccine production will be considered. These will include extracting candidate antigens from large-scale production of virus, identifying appropriate antigens and synthesizing them, insertion of appropriate genomes in bacteria or yeast for antigen production, insertion of appropriate HTLV-III genome segments into vector viruses, and synthesis of peptides of the viral envelope products.
- When candidate vaccine materials have been shown safe and antigenic in animals, Phase I clinical studies will begin in humans.
- Hyperimmune serum and monoclonal antibodies will be developed to determine their feasibility in treatment of AIDS and/or ARC.

Animal Models

The objective of these studies is to continue to develop animal models of AIDS in which candidate vaccines and drugs can be tested.

- Studies of naturally occurring animal retrovirus infections simulating AIDS, such as Simian AIDS.

- Studies on the transmission of HTLV-III from humans to nonhuman primates. These projects will attempt to establish a reproducible means to induce clinical manifestations of AIDS in nonhuman primates, in order to develop a better animal model for the disease. Such a model promises to provide investigators with means to assess the natural history of AIDS and evaluate a variety of interventive measures for the treatment or prophylaxis of human AIDS. Another aspect of these studies will be to mate infected or seropositive animals and study their offspring to further investigate maternal-fetal transmission of HTLV-III. Additionally, serial passage of HTLV-III will be made in chimpanzees, paralleling comparable studies of natural infections in man, to determine if antigenic drift occurs, an important factor in vaccine development.

Outreach

Information programs have been designed to promote a fuller understanding of AIDS and to disseminate the latest research advances to those involved in the care of AIDS patients. For example:

- A series of workshops, seminars, conferences, and outreach education programs aimed at different populations, including physicians, health care workers, allied service personnel dealing with AIDS patients, and lay individuals. As an example, NIAID has developed an outreach education program specifically designed for health workers and allied support personnel who care for AIDS patients. These conferences have been held in a number of U.S. cities, and the program will continue. The purpose of the conferences is to provide the most recent information and to dispel myths and fallacies regarding AIDS. One of the major thrusts of this effort is discussion of the known facts and fallacies associated with modes of transmission and protection, and the currently accepted guidelines for the proper management of patients with AIDS. NIAID also plans to develop workshops on AIDS for presentation at national professional and lay organization meetings.

o Current support by National Heart, Lung and Blood Institute to identify the most effective methods to inform and counsel blood donors who are identified as HTLV-III antibody positive will continue. Future activities in this area may include consensus development conferences on appropriate methods to counsel blood transfusion recipients, hemophiliacs, persons with sickle-cell disease or Cooley's anemia, and bone marrow recipients regarding their health status and lifestyle after exposure to HTLV-III.

o Use of the Physician's Data Query (PDQ) system developed by NCI as a means of providing physicians with information about standard and experimental treatment of cancer, locations of experimental treatment, and the names of cancer specialists. To respond to the AIDS crisis and make the most recent information on AIDS available to health practitioners, NCI has included information on ongoing AIDS studies in the PDQ system.

o Provision of information support by the National Library of Medicine (NLM) through bibliographic and reference services. NLM is producing a comprehensive bibliography on AIDS, which will be available both to the Department and to extramural AIDS investigators.

Summary

Mr. Chairman, I believe I have provided the Committee with an overview of NIH activities that demonstrate our major commitment toward developing treatments, a vaccine, and ultimately a cure for AIDS. The fast pace of AIDS research at NIH and in the numerous research institutions in this country and around the world, makes almost any research planning effort dated before it is complete. NIH research efforts directed toward the AIDS problem are both logical and comprehensive. Our efforts, fully coordinated with other agencies of the PHS, are broad and multifaceted, since no one can predict which approach will ultimately be successful. We all hope for new findings in this area, and are prepared to apply those results to our research effort upon discovery.

This concludes my prepared statement. I will be pleased to answer any questions you may have.

STATEMENT OF DR. DONALD R. HOPKINS

Mr. Chairman and members of the Subcommittee, I am Dr. Donald Hopkins, Acting Director of the Centers for Disease Control. I am pleased to appear before you today to discuss CDC's activities in Acquired Immune Deficiency Syndrome (AIDS) prevention and control during FY 1985 and our proposed activities in FY 1986.

When clusters of a rare cancer, Kaposi's sarcoma, and Pneumocystis carinii pneumonia were first recognized in homosexual men in 1981, CDC took a lead role in investigating these disturbing phenomena. As a result of early epidemiologic investigations, and in an effort to standardize reporting, a case definition was developed for what was to become known as AIDS. A nationwide surveillance program was established to monitor trends as the epidemic progressed, and specialized epidemiologic studies were initiated to investigate modes of transmission and to identify those factors and groups associated with increased risk for developing AIDS. CDC also joined in the laboratory search for the agent causing the disease.

Surveillance studies showed very early that AIDS was spreading rapidly in certain populations and that the disease would soon become a major public health concern. One important surveillance tool early in the AIDS epidemic was an increasing demand on the CDC drug service program for distribution of pentamidine isothionate, a drug used in the treatment of Pneumocystis carinii pneumonia. Pneumocystis is an infection most commonly seen in immuno-compromised patients. CDC had started distribution of pentamidine isothionate to treat Pneumocystis under an Investigational New Drug (IND) license in 1967. An increase in requests for this drug was noted in 1981 and by 1984 more than 350 patient doses were distributed each month, a clear indication of the increasing number of AIDS cases in this country. Because of increasing demand for this drug to treat AIDS patients, CDC and the FDA actively sought a U.S. producer and possible distributor for pentamidine in 1983. In November 1984, CDC discontinued distribution of pentamidine after the drug became commercially available.

Epidemiologic studies and investigations into individual cases by CDC defined certain populations at high risk for AIDS. These included sexually active homosexual and bisexual males, IV drug abusers, and recipents of blood and blood products, (especially patients with hemophilia). These findings strongly suggested that a bloodborne agent, probably a virus, was responsible for the disease. Laboratory studies identified imbalances in patients' immune systems, indicating that the white blood cells, responsible for defending the body against the disease, were being destroyed.

In order to speed research into this new disease, CDC became a major center for disseminating information. Through 64 articles thus far in its weekly publication, the Morbidity and Mortality Weekly Report, scientists around the world have been kept abreast of the latest developments in the field. CDC continues to be a major collaborating center for additional research.

Controlling the spread of AIDS also required assertive action at the State and local levels. Therefore, CDC collaborated with State and local health departments and other community groups whose organized participation was essential for success. Much of CDC's resources to date have been directed toward those States and communities with the highest incidence of AIDS. Collaborative efforts have been designed to enhance communitywide surveillance for AIDS, to protect the Nation's blood supply through the provision of alternate test sites, and to stimulate health education and risk reduction activities. We have also worked closely with a number of States and communities on epidemiologic research to answer some of the fundamental questions that currently constrain our mutual efforts to understand AIDS, clearly explain it to an increasingly concerned public, and begin to effect its control. In FY 1986, CDC will expand its cooperative relationship with State and local health departments and other community organizations on a broad national scale by providing the funds, the training, and the technical assistance to augment our mutual efforts to control the spread of HTLV-III virus.

During FY 1985, CDC has expanded AIDS surveillance, epidemiologic studies, and laboratory investigations, and has initiated major health education and risk reduction activities. Our total appropriation in FY 1985 for these activities, which I will discuss in more detail below, has been $33.2 million.

Surveillance

National surveillance of AIDS has been maintained and upgraded through mathematical modeling of current and future trends. The completeness of case reporting is being verified in several States and cities, and patients surviving over 3 years are being epidemiologically characterized. Special microcomputer software has been developed for use by State and local health agencies to assist in the analysis of AIDS surveillance information and to expedite reporting to CDC. Cooperative agreements are providing financial and technical assistance to 23 State and major city health departments for active AIDS surveillance.

Epidemiologic Studies

Current epidemiologic studies include investigation of blood donors in transfusion acquired AIDS cases, study of families of hemophiliacs and other AIDS victims, intensive investigation of patients outside the usual high risk groups, studies of transmission in Central Africa, and studies of health care workers who have had inadvertent needle stick injuries. One of these studies is following a cohort of 7,000 homosexual men in San Francisco to determine incidence, risk factors, and natural history of AIDS disease and infection. Another study is focusing on individuals transfused with blood from persons who later developed AIDS or AIDS-related conditions. We are performing a number of studies to determine the risk factors and determinants of spread in homosexual or bisexual men. Prevalence and transmission studies in prostitutes and heterosexual cases are also being initiated. We are intensively studying volunteer blood donors who are positive for HTLV-III/LAV. Laboratory support for these studies has also been provided, including characterization of the immune response to HTLV-III/LAV infection and development and evaluation of improved diagnostic tests and studies of new ways to grow the virus. We have determined the susceptibility of the virus to various disinfectants and are actively searching for an animal model of HTLV-III/LAV infection. AIDS laboratory training has been conducted for 117 State and local laboratory personnel.

Prevention: Health Education and Risk Reduction

In anticipation of FDA's licensure of a serologic test for antibodies to HTLV-III/LAV (which occurred on March 2, 1985), CDC conducted 44 1-day seminars in 34 cities on HTLV-III/LAV antibody testing during February 1985. These seminars brought current information about the test and its interpretations to over 7,500 health workers. CDC followed these seminars by spending $10.4 million to implement alternative site testing in the States. These sites were intended to help protect the Nation's blood supply by providing an alternative to blood banks and plasma centers for those persons wishing to know if they had been infected with HTLV-III/LAV. By presenting a two-day course during 35 sessions in 28 States, CDC prepared health workers to counsel patients at these alternative sites. More than 30 additional courses were taught by State and local health department staff who had been trained by CDC instructors to use the CDC curriculum and training materials. We also assisted the Association of State and Territorial Health Officials in producing a guide on the management of alternative site testing. At present, HTLV-III/LAV antibody testing is available in 518 alternative sites in 52 States and Territories. Use of alternative testing sites has been lower than anticipated. Volunteered provisional data from several sites suggest a positivity rate of 10-20%. This initiative has served its mission to help protect the nation's blood supply.

CDC has been operating a national hotline which answers more than 700 calls daily from the general public on AIDS and makes appropriate referrals for further information. We also awarded a total of over $1 million to 6 of the areas with the highest AIDS morbidity to conduct activities that provide risk reduction information to the public and attempt to influence the behavior of those at highest risk for AIDS. CDC is about to award approximately $1.2 million in cooperative agreements to demonstrate the impact of current health education and risk reduction methods, and to test innovative approaches to prevent the spread of AIDS.

CDC continued a cooperative agreement with the United States Conference of Mayors to help fund the grass roots AIDS health education and risk reduction efforts of 19 community-based organizations. The conference also publishes a monthly AIDS Information Exchange, which provides 800 of the nation's mayors and their local health officials with timely, accurate information about AIDS. Finally, CDC funded a study of the nature, scope, and evaluability of AIDS health education and risk reduction efforts conducted to date in 9 large cities, and is preparing reports of that study in collaboration with representatives from local public health and community organizations conducting AIDS health education.

FY 1986 Budget Amendment

The President's FY 1986 Budget request asks for $45.6 million for AIDS activities at CDC. This request includes an amendment for $26.925 million. With these funds, CDC will continue and expand many critical activities initiated in FY 1985, in accordance with the Public Health Service's Plan for the Prevention and Control of AIDS. That plan calls for continuing to clarify the epidemiology and natural history of HTLV-III/LAV infection and AIDS, continuing to implement national and community risk reduction and information programs as early prevention and control measures, designing and evaluating improved prevention and control measures, and designing and promoting prevention and control programs that grow in effectiveness through incorporation of new intervention tools (vaccines/antivirals) as they become available. Particular attention will be paid in FY 1986 to the role of heterosexual transmission, determination of the incidence of new HTLV-III/LAV infections, persistence of virus in bloodstreams of infected individuals, and enhancement of State and local efforts to reduce transmission through education and risk reduction. The remainder of my statement will focus on the 1986 budget amendment for CDC and the activities it will support.

Surveillance

Approximately $2.4 million will be used to expand our surveillance activities. CDC will attempt to define the magnitude and trends of infection and disease in several special groups and geographic areas through such methods as comparing reported incidence of AIDS by risk group to incidence and prevalence of infection in these groups. Laboratory proficiency for HTLV-III/LAV testing in States and local laboratories will be examined. The sensitivity and specificity of commercial blood tests will also be studied.

Epidemiologic Studies

CDC plans to use $3.825 million to expand epidemiologic studies to determine the role of specific sexual practices and other potential risk or protective factors influencing heterosexual transmission; compare frequency of sexual transmission from female to male with that from male to female; document the prevalence of infection in prostitutes and correlate these findings with history of IV drug usage and other factors; evaluate the risk of spread in day care centers and hospitals; and study the spread of the virus among households in Zaire to clarify risk factors for transmission among spouses, siblings, parents and children living in households of infected persons. Results from these studies are expected within the next 1-3 years. Laboratory efforts will continue to provide training and backup support to States, characterize the virus and the immune response to it, and emphasize comparison of the human response with that observed in animal models.

Prevention: Health Education and Risk Reduction

Until a vaccine and/or therapy for AIDS is developed, the only prevention program available is health education/risk reduction. The Budget Amendment includes $20.665 million to reduce transmission through education which is aimed at encouraging high risk individuals to change related aspects of their behavior. CDC plans to spend $5.4 million to assist States in building a core capacity directed toward the prevention of AIDS and the transmission of HTLV-III/LAV infection. When new scientific findings and health education/risk reduction approaches are developed, the States would then have the systems in place to rapidly disseminate the new prevention strategy. In addition, fifteen of the highest morbidity areas will receive approximately $7.8 million to intensify their prevention efforts, and implement evaluation mechanisms to monitor their effectiveness. These programs will be designed to assure the provision of targeted education for groups and individuals at high-risk, and to educate them regarding specific risk reduction practices. They will also assure the provision of risk reduction counseling programs to develop the individuals' ability to make needed behavioral changes and will assist in assuring community support of lifestyle changes.

To determine the most effective health education/risk reduction programs and techniques, demonstration and evaluation projects will be funded for approximately $4.2 million in 3 or 4 States/cities to support intensive projects for prevention of AIDS and HTLV-III/LAV infection. The evaluation of the effectiveness of the educational programs will be accomplished through surveys to document changes in the understanding of the AIDS (HTLV-III/LAV) risk factors, and to evaluate changes in risk-associated behavior and infection rates resulting from program efforts. Trends will also be monitored in other illnesses which are sensitive indicators of behavior change in high-risk populations (e.g., reportable sexually-transmitted infections, hepatitis B and non-A, non-B, etc.). Information gained from these demonstrations will be shared promptly with all States to increase the cost-effectiveness of their ongoing activities.

To stimulate new approaches to community health education/risk reduction programs, CDC will award $2 million to encourage unique and innovative approaches to prevent and/or control transmission of HTLV-III/LAV infection. Approximately ten projects will be supported in academic institutions, community organizations, public health departments, and other organizations for new approaches to prevent and/or control transmission of this disease and to evaluate their effectiveness.

Finally, included in the requested amendment is $1.265 million for technical assistance to the States to help them improve program effectiveness and reduce cost. The assistance will include national strategy planning; refinement of risk reduction guidelines; development of demonstration and evaluation projects; development of uniform evaluation guidelines and

instruments; expanded support of the Hotline; and provision of training to health department and community personnel.

It is clear that AIDS continues to be the Nation's highest public health priority. In the absence of an effective treatment or vaccine, we intend to do all we can in the areas of surveillance, epidemiology, and health education in order to reduce the transmission of this virus.

This concludes my statement. Mr. Chairman, I'll be glad to try to answer any questions you or other Senators may have.

STATEMENT OF DR. DONALD IAN MACDONALD

Thank you for the opportunity to appear here today to discuss the role of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) in the Department of Health and Human Services' efforts dealing with Acquired Immunodeficiency Syndrome (AIDS).

ADAMHA is vitally involved with the U.S. Public Health Service (PHS) effort to prevent and to control AIDS. Although the major risk group for AIDS is homosexual and bisexual men, approximately 17% of all AIDS patients are intravenous (IV) drug users. In addition, another 8% are both IV drug users and gay or bisexual men. Psychosocial consequences are common for both the AIDS patient as well as for those with known HTLV-III infection, the causative agent for AIDS. More than 50% of AIDS patients develop dementia and/or psychosis during the course of their illness and one in five of these demonstrate neurocognitive and behavioral change before the diagnosis of AIDS is confirmed. These clinical observations, are presumed secondary to a direct viral infection of the brain with HTLV-III.

As part of the PHS effort to prevent and control AIDS, ADAMHA will focus activities in three areas: (1) epidemiologic investigations; (2) prevention and control recommendations; and (3) risk reduction programs. Furthermore, it will collaborate with the National Institutes of Health and the Centers for Disease Control in efforts to monitor the incidence of AIDS, to establish the diagnostic criteria for AIDS, to maintain surveillance of ARC, and to prepare AIDS information relevant to the psychosocial and drug abuse aspects of AIDS. ADAMHA AIDS activities are coordinated through the Subgroup on Psychology, Psychiatry, and Addictive Aspects of AIDS, part of the PHS Executive Task Force on AIDS. My personal involvement as Chairman of this Subgroup affirms the importance ADAMHA places on AIDS as a health priority.

In addition, the Agency strategy and implementation plans to prevent and to control AIDS include: preparation of educational and informational materials for drug abusers and for health care personnel caring for them; preparation of a monograph directed towards the health care worker addressing the psychosocial needs of AIDS patients and persons infected with HTLV-III; and research into epidemiologic and neurobehavioral aspects of AIDS. To date ADAMHA has provided support for research on AIDS totaling $6.5 million dollars. Areas of investigation include the prediction of sexual behavior change in high-risk groups for AIDS, epidemiologic studies of AIDS among IV drug users, psychoimmunologic correlates of AIDS, and interactions between psychoactive drugs and viral illness outcome. Two ADAMHA Institutes, the National Institute on Drug Abuse (NIDA) and the National Institute of Mental Health (NIMH) have primary roles in our AIDS activities.

NIDA's current efforts are directed towards assessing the spread of HTLV-III exposure, AIDS, and AIDS-related complex (ARC) among the drug using population and towards addressing the needs in drug users already infected by HTLV-III, or symptomatic of AIDS. The Institute's activities have focused on three principal populations: (1) drug users currently infected with HTLV-III; (2) other drug users at high risk of and concerned about the disease; and (3) drug abuse treatment and service providers. The Institute is also concerned with developing more effective prevention measures which will incorporate the increased knowledge about this disease and assist in stopping the spread of AIDS to other populations.

To accomplish these goals, NIDA intends to continue all ongoing prevention activities and information dissemination efforts. Specifically, NIDA has supported work which endeavors to:

o Clarify the epidemiology and natural history of HTLV-III infection in IV drug users. Studies have examined samples in both high and low prevalence areas for AIDS in IV drug user population. Studies of the interaction of drugs of abuse and immune function hold great possibilities in clarifying the possible co-factor role of these agents in the course of AIDS.

- Stimulate and conduct research and development of effective prevention approaches and treatment agents. NIDA efforts center on research related to HTLV-III disease among the drug using population. In addition to epidemiologic studies (e.g., etiology, risk factors, and natural history), NIDA has stimulated research on effective prevention and intervention strategies to determine their efficacy in reducing the spread of HTLV-III disease among the drug-using population.

- Implement national, State, and community risk prevention and education programs as prevention and control measures. NIDA continues to develop and disseminate information aimed at reducing the incidence of HTLV-III and to disseminate information to specific high-risk subgroups and the general public about the relationship between drug abuse, the spread of HTLV-III, and the subsequent development of AIDS and AIDS Related Complex.

- Design and evaluate improved prevention and control measures. NIDA is striving to expand its knowledge transfer and technical assistance activities aimed at better informing drug abuse treatment providers about methods and procedures most suited for serving drug abuse clients infected with, or at risk for HTLV-III disease. Efforts are aimed at engaging in drug abuse treatment, and/or other appropriate medical programs, drug users who have AIDS or other stages of HTLV-III infection or at high risk of contracting and/or spreading HTLV-III. Because there are significant geographic differences in the incidence of AIDS among IV drug users, control programs recommended may vary from State to State.

NIMH's current efforts are directed toward understanding and assessing the psychiatric, behavioral, and psychosocial aspects of AIDS. This includes identifying those persons most at risk for the development of AIDS, identifying those psychological and behavioral factors which may negatively or positively influence the course of the illness, and identifying the relationship between the immune function and mental health status, such as depression, anxiety, or responses to high levels of stress. Specific activities of the Institute include:

- Support of investigations of mental health risk factors as they relate to the incidence of AIDS. Because of the limited knowledge currently available regarding mental health aspects of AIDS, ARC, and HTLV-III exposure, NIMH provides support for projects focused on the psychiatric, biobehavioral, neuropsychologic, and psychosocial aspects of AIDS. Investigators supported by the Institute are developing neuropsychologic instruments specific to AIDS patients; identifying those factors predictive of sexual behavior change associated with the AIDS epidemic; delineating the different psychologic responses of the AIDS, ARC, and HTLV-III patients; and studying the cognitive change associated with and antecedant to the development of AIDS.

- Implement national, State, and community risk prevention and education programs as early prevention and control measures. NIMH continues to develop information on mental health consequences of AIDS. In addition, the Institute will direct research and dissemination efforts toward specific population groups, such as health care providers, care givers, and community-based AIDS organizations. The information includes knowledge of the psychological and psychosocial issues related to those in high-risk groups, those in contact with AIDS patients, and those with AIDS or AIDS Related Complex as well as the medical/psychiatric complications of HTLV-III and their clinical manifestations such as delirium and dementia. These dissemination activities continue to be conducted through a variety of mechanisms including press, media, and national professional association contacts and efforts to work with local radio and television to develop education programs for the general public.

Mr. Chairman, this concludes my formal statement.

STATEMENT OF DR. FRANK YOUNG

I welcome this opportunity to be here with my other colleagues from the Public Health Service (PHS) to discuss this most important public health issue with you.

Before describing the Food and Drug Administration's (FDA) role in combating the AIDS epidemic, I want to commend Dr. Jim Mason for his outstanding leadership during this very difficult time. I wholeheartedly support his efforts in coordinating the PHS research, prevention, and control strategies against Acquired Immunodeficiency Syndrome (AIDS).

The FDA's role in the PHS's activities relative to the AIDS epidemic is based on FDA's responsibility to oversee approval of safe and effective drugs and devices. Thus, we are responsible for the safety of the blood supply through licensure of blood and plasma collecting facilities, development of regulations for the manufacture of blood products and licensure of the products themselves. The FDA is also responsible for monitoring the use of investigational new drugs, including therapeutic substances and vaccines, in humans and for approving and/or licensing these products for marketing. Furthermore, our research scientists have also joined with others in a massive research effort to identify therapeutic modalities to treat the disease and to develop a vaccine to prevent it.

SAFETY OF THE BLOOD SUPPLY

Once it became evident that AIDS could be transmitted through blood and blood components, it became essential to take steps to enhance and ensure the safety of the nation's blood supply.

To this end, one of the first actions undertaken was the development of criteria for identifying and excluding prospective blood and plasma donors at increased risk of transmitting the disease. These screening criteria have been in use in blood banks and plasma centers since the FDA issued its original directive to the blood and plasma facilities in March 1983. This guidance has been continually reviewed and was updated in December 1984 and, most recently, on September 3rd, as new information became available to us. I will provide these for the record. The identification and exclusion of high-risk donors actually predated the isolation of the HTLV-III virus, the causitive agent for AIDS. Thus, the criteria relied entirely on the epidemiological data available at that time, and the success of the program can be attributed to the voluntary cooperation of high-risk groups.

ANTIHEMOPHILIC FACTORS

In addition, important advances were also made in the area of improving products used for the treatment of hemophilia prior to the isolation of the HTLV-III virus. Our FDA scientists working with those in industry were able to develop new heat and chemical treatment techniques that inactivated the virus while retaining the biologic activity of the antihemolytic factors VIII and IX.

HTLV-III ANTIBODY TEST FOR SCREENING BLOOD AND PLASMA

After the etiologic agent HTLV-III was identified, it became possible to develop a test for general use which would detect the presence of antibodies to that virus in the blood. To move as rapidly as possible toward an antibody test, Secretary Heckler announced that the Government would transfer the technology developed at the National Cancer Institute to the private sector. The potential existed there, not only for mass production of the test, but also for product improvement and refinement.

The companies selected to further develop and produce the HTLV-III antibody test made remarkable progress and, earlier this year in March and April, the FDA licensed several companies to market the test. The universal application of the HTLV-III antibody test to screen all blood and plasma, a test which has now proven to be highly sensitive and specific, has added immensely to our ability to ensure the integrity of our nation's blood supply and to assist our research efforts toward prevention and treatment of AIDS.

Thus, the antibody test, coupled with the heat and/or chemical treatment of certain blood products and the blood donor exclusion criteria for high-risk individuals, have virtually eliminated the risk of transmitting HTLV-III by blood and blood products.

PUBLIC/PRIVATE SECTOR COOPERATION

Let me diverge here on what is surely a significant contribution to the progress which has been realized in combating this dreadful disease. To progress from isolation of the virus to the development, mass production, licensure and application of a new technique in less than a year's time is a remarkable scientific achievement. This was due in no small measure to the fact that at FDA we had an excellent team of scientists that were able to work with industry, the blood service community, the NIH and the Centers for Disease Control (CDC) in speeding the translation of the initial discovery into the availability of practical products. The advances we have made have been possible only because of everyone's quick and concentrated response to a disease that did not even exist five years ago. Scientists and physicians of the PHS and their colleagues here and around the world have cooperated in a massive research effort and these dedicated researchers will continue until AIDS is under control.

In order to achieve these milestones, it was necessary to share information which would normally be kept in the strictest confidence within industry, so that the greater interest of the public health could be served. I cannot emphasize enough how vitally important this point is and the cooperation demonstrated by all involved.

PUBLIC HEALTH SERVICE COORDINATION

Under the overall guidance of the PHS Executive Task Force, specific committees were established at both the National Institutes of Health (NIH) and FDA to deal with therapy and prevention and blood safety. There has been close interaction and participation between these groups at the working staff level.

The groups meet regularly to coordinate the screening and clinical testing of products which are identified as being potentially useful for the treatment of AIDS. This coalition of talent and interagency dialogue will help to ensure the evaluation of new AIDS therapies in patients as promptly as is scientifically and ethically appropriate and will allow for an efficient mechanism to be in place to share the results broadly within both the medical community and the general public.

PROFESSIONAL AND PUBLIC EDUCATION

The PHS's role in keeping the public informed has been of the utmost importance because of the many misconceptions prevalent about the disease. With respect to specific areas under our jurisdiction, we have worked with NIH and CDC to disseminate information which was rapidly developing and changing. Several public workshops and conferences have been held. One took place at NIH on February 22, 1985, shortly before licensure of the new antibody test, so that health care professionals and the general public would have an opportunity to understand what the new test would be able to do. Another was held on July 31st to discuss the data generated in blood and plasma facilities in their first several months of experience with the use of the test. It was at this conference that participants recognized that use of the test, along with the donor exclusion criteria, had virtually eliminated the risk of transmitting HTLV-III through the nation's blood supply.

Additional efforts to keep the health care community as well as the general public informed included my February 19 Dear Doctor letter to 530,000 physicians. This letter disseminated PHS's provisional recommendations for screening donated blood and plasma for antibodies to the HTLV-III virus and other timely AIDS information directly to health care professionals.

Also, several FDA Drug Bulletin articles and an FDA Consumer article have been published. A special edition of the Drug Bulletin devoted entirely to this issue will be published within the next week. Through this edition, prepared in cooperation with NIH and CDC, we will be able to bring one million health professionals, including all of the nation's physicians, up to date on this important public health matter. A second FDA Consumer article is also being prepared.

AVAILABILITY OF TREATMENT

Let me now turn to an issue of tremendous import. We are all painfully aware of the desparate efforts of the victims of this devastating disease to seek treatment. Unfortunately, no cure exists, but enormous efforts are being made on all fronts to find a way to treat, cure and prevent AIDS. As I mentioned earlier, FDA and NIH are working closely to facilitate the development and evaluation of any therapeutic agent which appears to be promising. These efforts are directed toward the screening and testing of antiviral products, products which will stimulate the immune response, the development of a vaccine against the AIDS virus and drugs which will be effective in the treatment of the opportunistic infections associated with AIDS.

In order for clinical testing to proceed with products intended for use in the treatment of AIDS (or any other condition), an Investigational New Drug (IND) application is filed with FDA. The IND must contain information needed to demonstrate the safety of proceeding to test the drug in human subjects, including drug composition, manufacturing and control data, results of animal testing, training and experience of investigators and a plan for clinical investigation. In addition, assurance of informed consent and protection of the rights and safety of human subjects is required.

The initial clinical use of investigational drugs (Phase I) is intended to carefully assess the safety of the drug and to determine any pharmacologic effects that can be monitored. The number of patients entered into these pilot trials is necessarily limited until the initial assessment of toxicity is determined. As data are accumulated, studies are gradually expanded in scope and size to obtain safety and efficacy data to support marketing of the drug (Phases II and III).

The FDA has expedited the handling of all requests for the study of experimental agents for this condition. The FDA has met on one or more occasions with every manufacturer who has expressed an interest in submitting an IND for the use of a product in AIDS or AIDS-related complex to discuss the procedures for filing an IND. In some instances, the FDA has initiated contact with manufacturers who have a drug that shows some activity in the laboratory against AIDS, to offer our assistance in guiding them through the drug development process.

Also, in several instances, promising treatments relevant to AIDS have gained orphan drug status. Perhaps the best example of FDA's helping hand in the drug development process is with pentamidine, a drug which effectively treats a fatal form of pneumonia that often strikes AIDS patients and others with disorders of the immune system. Scientists at the CDC, FDA, and the company worked closely to ensure the continued availability of this life-saving drug to patients in the United States, and the drug was approved in October 1984. FDA and CDC even conducted some of the laboratory and clinical work necessary to get the drug approved. More recently, the antiviral drugs HPA-23, BW-A509U and BW-D759U were also granted orphan drug status.

The FDA has offered its assistance to expedite and facilitate the filings of INDs to foreign as well as domestic firms. As you may know, the manufacturer of HPA-23 which has been used in France recently applied for and received FDA permission to begin limited clinical trials in the United States with this drug. The studies are scheduled to begin at selected U.S. medical centers within the next few weeks.

Again, I must emphasize that the availability of promising new products is a result of the cooperation of industry and the bioresearch community and their willingness to share confidential data and information under circumstances which do not usually exist at this stage of drug development. In addition, the drug manufacturer's straight-forwardness in allowing us to indicate sites where legitimate clinical testing will be conducted will help to eliminate any fraudulent use of the drug and, consequently, the exploitation of patients who are already suffering enough.

In these meetings with company officials, FDA scientists have discussed the information necessary for inclusion in the IND request. They have also assisted in the design of the clinical plan so that studies on drugs which might prove to be useful therapeutic modalities for AIDS could be initiated rapidly once the IND is filed.

With this joint effort between FDA, NIH, manufacturers, and academic scientists, approval for a newly filed IND can be granted in a matter of days, and amendments to the original protocol agreed to by telephone as all parties work together to closely monitor the progress of patients under study.

We have also met with leaders of several of the high-risk communities regarding treatment and prevention. We will continue these efforts so that we will benefit from their input and help since they will be the primary research subjects.

Of the drugs currently in clinical trials in AIDS patients, there are not yet sufficient data to establish their effectiveness in the treatment of AIDS. There are a few compounds, however, for which there is some preliminary clinical evidence of possible usefulness in the treatment of AIDS or opportunistic infections. But, I must point out, that a number of the antiviral drugs may have significant toxicity. In the case of the immune system modulators, there is the danger of providing an enhancement to viral replication and shortening the time of disease progression. Nevertheless, despite the vagaries and complexities of clinical investigations in a disease in which the natural history is not entirely understood, we are prepared to review expeditiously all investigational and marketing applications for products for AIDS, AIDS-related complex and opportunistic infections as we have for HPA-23 and as we are now doing for the recently filed new drug application for isoprinosine.

Consequently, the prudent scientific procedure is to make initial observations on these drugs on a limited number of patients until the toxicity question is resolved and some therapeutic action established before moving on to larger trials. This procedure speeds the acquisition of necessary data and minimizes the risk for patients.

I wish to stress that we remain most concerned about facilitating the availability of any product that appears to be useful in treating AIDS victims and alleviating the suffering it causes, and we are prepared to work with anyone willing to sponsor clinical investigations consistent with our obligations to safeguard patients used as research subjects.

OTHER ACTIVITIES

In addition to our role in the oversight of the conduct of the clinical trials and issues relating to the safety of the blood supply, FDA scientists in FDA laboratories on the NIH campus collaborate with other groups involved in AIDS research. They are participating in the in vitro screening of antiviral drugs and immune stimulators and in the evaluation of patients on experimental treatments at the NIH Clinical Center.

FDA is also working with NIH in areas related to vaccine development. Here the development of animal models capable of measuring the immunogenicity of HTLV-III component proteins is important. The skilled virus research teams on FDA's staff will help in the development of such a vaccine.

This integration of FDA into the total AIDS effort guarantees that, as was the case with the HTLV-III antibody test, any promising product will get rapid regulatory review and become generally available in the shortest possible time.

BUDGET REQUEST

I appreciate the opportunity to testify before this Subcommittee. As you know, the FDA falls under the jurisdiction of the Appropriations Subcommittees on Agriculture and Related Agencies in the Senate and House. Fortunately, these Subcommittees and their chairmen have been extremely responsive whenever we have come to them with requests for funds urgently needed to cope with significant public health problems. In fact, Mr. Whitten personally sponsored a floor amendment to include an additional $2,145,000 to support other additional AIDS activities for FDA in FY 1986. This amendment was passed, and these resources were included in the Appropriation Act passed by the House on July 24. I am also pleased to report that this amount was also included in the bill reported out of the Senate Appropriations Committee on September 24. Let me now briefly discuss with you our plans to utilize these resources in 1986.

During the past 12 months, several major developments relevant to the transmission, prevention, and control of HTLV-III infection and AIDS have occurred. Serologic tests to detect HTLV-III antibodies have been licensed, and the tests are being used to screen donated blood and plasma. Furthermore, a number of therapeutic products have been entered into clinical trials and are under active investigation.

The pace of these developments requires that FDA expand its surveillance and monitoring efforts. Activities undertaken as part of this request will increase our knowledge regarding the screening tests that enhance our ability to assure the safety of the nation's blood supply; and expand the capacity for review and approval of new diagnostic and treatment products.

Specific projects will include:

-- Followup and evaluation of blood donors who are found positive by the HTLV-III screening test to determine the medical significance of the result for the individual and the risk associated with blood donations from persons who have developed antibody to HTLV-III.

-- A study of the impact of additional tests for HTLV-III virus and other retroviruses on the safety of the blood supply.

-- A study to determine whether HTLV-III is present in feces to investigate transmission in animal models.

-- Additional quality control monitoring of test kits for HTLV-III.

-- Review and approval of second and third generation tests for AIDS, including tests for viral components, and evaluation of diagnostic and treatment products, including an eventual vaccine against the HTLV-III virus.

-- Development of adequate methods for collecting and analyzing adverse reaction reports associated with drugs and biologics which come into use for the prevention and treatment of AIDS.

CONCLUSION

In closing, I can only say that this dreaded disease has presented challenges which have been unprecedented and unparalleled in anyone's memory. However, we are proud of our accomplishments and will diligently pursue our goals of improving and refining the existing blood test, discovering and making effective treatment available, and developing a vaccine to prevent AIDS. We pledge to continue to work with our sister agencies in the PHS in our quest to conquer this devastating disease.

This concludes my prepared statement, Mr. Chairman. I would be happy to answer any questions you might have.

SUMMARY STATEMENT OF DR. JAMES MASON

Dr. MASON. Thank you, Mr. Chairman. We are pleased to have this opportunity today to discuss the Public Health Service's efforts in combatting the epidemic of AIDS and to review our financial commitment to those efforts.

In my brief remarks, I would like to review what we have learned about AIDS since 1981 and outline how we have used this knowledge to act responsibly, rapidly, and to plot future strategies. Four PHS agencies—ADAMHA, CDC, FDA, and NIH—have made significant contributions to our understanding of this problem, and I am delighted to have accompanying me Dr. Donald Macdonald, head of ADAMHA; Dr. Donald R. Hopkins, Acting Director of CDC; Dr. Frank Young, who is Commissioner of the Food and Drug Administration; and Dr. James Wyngaarden, Director NIH. In their testimonies, each will describe the efforts underway and the agency's plans for both the request made in the fiscal year 1986 budget as well as those made very recently for supplemental funds.

The activities of these agencies are coordinated through the PHS executive task force on AIDS chaired by the Assistant Secretary for Health. This group meets biweekly. It is an important forum within the Public Health Service to communicate, coordinate, review policy, and to formulate plans for combatting this disease.

Within this task force, four subgroups are charged with working within specific areas. These include the following:

Vaccine development and therapeutic intervention, which is chaired by Dr. Wyngaarden;

Epidemology and prevention, which is chaired by Dr. Hopkins;

Blood and blood products, which is chaired by Dr. Harry Myer of the Food and Drug Administration;

And the psychological, psychiatric, and addictive aspects, chaired by Dr. Macdonald.

Through these four subgroups, the agencies within PHS coordinate their efforts in a number of areas, including blood donor studies and development of animal models. In testimony of the agency heads, you will hear of the role each agency plays in these activities. There are also three panels of the PHS executive task force on AIDS which coordinate activities on information development, resources, and science.

Acquired immunodeficiency syndrome is a disease of epidemic proportions and is a national health problem unprecedented in recent history. Secretary Margaret Heckler has made control of this disease our No. 1 public health priority.

As you know, the first cases of AIDS were reported to CDC in June 1981, although we now believe that the onset of the disease in the United States may go back to 1977. We do not know its origins. Some recent studies suggest that the disease existed in Central Africa in the early to mid-1970's. The number of AIDS cases reported in the United States has doubled each year, as shown in chart 1 of my testimony, if I can refer to that.

We now know of over 13,000 reported cases, but we believe that as many as 500,000 to 1 million persons in the United States are infected with the AIDS virus. Studies in homosexual men infected with AIDS virus indicate that 5 to 10 percent will develop AIDS within 2 to 5 years after becoming infected. The case fatality rate among AIDS patients is high. Over 50 percent of reported cases are known to have died.

For those diagnosed with AIDS for 2 years or longer, the mortality rate is over 85 percent.

There is no doubt that the principal mode of transmission is through sexual contact. Chart 2 in my testimony shows that nearly 75 percent of the AIDS cases among adults are related to sexual transmission. Most of these cases, about 74 percent, have occurred among homosexual or bisexual males. Another 1.2 percent have occurred among heterosexual partners of high-risk groups.

Another major mode of transmission is through sharing of needles among IV drug abusers. This mode accounts for from 17 to 25 percent of cases reported nationally. There is some overlap between homosexual men who use IV drugs. The risk for transmission of the AIDS virus through transfusion of blood or blood products, which in the past accounted for 2.2 percent of AIDS cases, or through transfusion of clotting factor, 8 percent of cases, these cases have been virtually eliminated. This is because a screening test, which detects antibody to the AIDS virus, is now used routinely by blood banks and plasma centers.

In addition, *routine heat and chemical treatment render clotting factor* free of the virus. In March 1983, the PHS issued guidelines recommending the voluntary avoidance of donation of blood and plasma by members of high-risk groups. Continued enforcement of these guidelines by centers provides an added layer of protection from acquiring AIDS through transfused blood, blood products, or clotting factor.

We now know that infected mothers can transmit the virus to their babies across the placenta and, likely, through breast milk. Although the AIDS virus has been isolated from human saliva and tears, there is no evidence that transmission has occurred through these routes.

There has not been a single case of AIDS reported to us in family members of AIDS patients, except for sexual partners and children born to infected women. In studies of over 300 household contacts, not one person—other than sexual contact or a child born to an infected mother—has become seropositive or developed AIDS as a result of living with AIDS patients.

In studies of more than 1,400 health care workers who have close contact with very ill, often hospitalized AIDS patients, not one has developed AIDS or become seropositive as a result of contact with patients, other than through needle stick injury. We continue to strongly urge people handling needles to observe the precautions PHS published in November 1982. These studies allow us to say with a high degree of certainty that the AIDS virus is not spread through casual contact. This would include sharing of meals, coughing, or sneezing.

We have done our utmost to get this message across to the public and the press in the past few weeks as concern has mounted about schoolchildren with AIDS.

Chart 3 shows our progress to date in combatting this disease. It has been remarkable the progress that has been made, although it is far from finished. We know who is at risk and how the disease is transmitted. The weekly publication of CDC, "Morbidity and Mortality Weekly Report," is one of our most rapid channels of communication to the Nation's public health community. In over 64 AIDS-related articles, the MMWR has carried our recommendations dealing with safety of the blood supply, personal behavior as a preventive measure, and use of the blood screening test.

On August 20, we recommended that in general, school-age children with AIDS should be allowed to attend school while proposing a more restricted environment for younger children with the disease. These guidelines are provided to assist State and local decisionmakers.

In addition to using the MMWR to assist State and local decisionmakers, we use it as a vehicle for communicating to the public health community, we have embarked upon a major plan for the prevention and control of AIDS and an outline of this plan has been published in the "Public Health Reports," the official journal of the Public Health Service.

We understand the cause of AIDS. In 1984, a retrovirus, human T-lymphotropic virus, type III. was identified as the cause of this disease. It is unusual to have the cause of a disease identified so quickly, especially, as in the case of AIDS, where the discovery of a new agent was involved.

Discovery of the AIDS virus allowed us to develop a test for use in blood banks and plasma centers to prevent transmission of the disease through transfusions of blood and blood products. The HTLV-III antibody test is now used to test every unit of blood or plasma in the United States.

Heat and chemical treatments were developed to render clotting factor essentially free of AIDS virus, and as a result, hemophiliacs are provided an added layer of protection from acquiring the disease. Because of the long incubation period of AIDS, however, we will continue to hear of new cases in hemophiliacs and recipients of blood transfusions who were infected before the HTLV-III antibody and other preventive measures were available.

Regrettably, as you have said, there is no currently effective treatment for those with AIDS, other than treating the opportunistic infection. We have screened over 100 drugs and a number of them are in various stages of clinical testing. You will hear from Dr. Wyngaarden and Dr. Young of their efforts to discover and bring to the market drugs of promise.

Vaccine development is underway, but our initial optimism at having a vaccine within a short time after the discovery of the HTLV-III virus has been stymied. The antibody that forms the basis of the blood test is not the one that protects against the disease. The development of a vaccine will require additional basic research.

Neither a vaccine nor an effective treatment is on the immediate horizon. But we do know enough about the transmission of AIDS to substantially curtail the spread of the disease if current knowledge were applied. Choice of personal behavior is a powerful tool for control of this disease.

Accordingly, we have accelerated our public information and education effort to advise Americans of the current information about transmissibility and the behavioral preventive measures they can take. Many communities throughout the United States are already actively involved in programs aimed at prevention and control of AIDS. Other communities need encouragement. We will continue to work closely with State and local health departments and other community groups.

Last week at a press briefing, I made the following recommendations. We will continue to promulgate these messages:

First, do not have sexual intercourse with AIDS patients, with members of the risk groups, or with people who are positive for the AIDS virus. But if you do, it would be prudent to use a condom and avoid sexual practices such as anal intercourse that may injure tissue.

Second, do not use IV drugs. But if you do, do not share needles.

Third, women who are sex partners of risk group members or who use IV drugs should consider the risk to their babies before pregnancy.

In fiscal year 1986, we have requested $126.3 million for our AIDS effort. I should note that $6.6 million of the total request is for FDA, whose budget is considered by the Appropriations Subcommittee on Agriculture and Related Agencies. The fiscal year 1986 request includes a $40.7 million increase over the original fiscal year 1986 President's budget which was submitted to the Congress in February of this year. And that is outlined in our chart 4.

The need to increase spending for AIDS was communicated by Secretary Heckler in a July 19 letter to the Appropriations Committee. This was followed up by a formal budget amendment on September 9, 1985. These resources will significantly enhance our ability to implement a major preventive strategy through the initiation of community health education/risk reduction programs throughout the Nation.

They will expand the NIH efforts toward identifying and testing antiviral compounds and developing a vaccine and they will expand necessary epidemiologic studies and surveillance activities.

The resources for AIDS have grown from a level of $5.5 million in fiscal year 1982 to $126.3 million in fiscal year 1986. That is detailed in chart 5. The PHS resource level has grown as the Department has identified opportunities for expanding its efforts against this disease.

The PHS, through its executive task force on AIDS, continually monitors plans versus accomplishments, and solicits the identification of new avenues for accelerated progress in controlling this disease. Because of the changing dynamic nature of the PHS effort to conquer AIDS, this monitoring process permits us to explore and pursue every reasonable opportunity to bring this disease under control.

The previously mentioned $40.7 million increase in spending resulted from a reassessment which was conducted during the spring of this year. Another reassessment of the AIDS effort was recently completed and, as a result, we believe there is a need to expand beyond our current request in order to evaluate new drugs and therapies and to gain a better understanding of the prevalence of AIDS.

In conclusion, I want to express my appreciation for the support this subcommittee has shown the Public Health Service as we move to learn more about AIDS and eventually preventing and treating this disease. As I have noted, the nature of this disease has required us to revise our spending estimates often in midyear. This subcommittee's willingness to work with us on this matter and your favorable response to our proposals have made our tasks as scientists and public health administrators less burdensome and contributed to the rapid pace of research and public education in this field. I am sure that as we proceed into fiscal year 1986, we will continue to work together as we review the progress we have made in combatting this disease and the opportunities for new inroads. Thank you.

Senator WEICKER. Dr. Mason, thank you very much. I intend to move on to other witnesses, except in your testimony you said, "Another reassessment of AIDS efforts was recently completed and, as a result, we believe there is a need to expand beyond our current request in order to evaluate new drugs and therapies." Could you give me an indication as to what that amount is going to be?

Dr. MASON. We have forwarded to the Secretary and from the Secretary to OMB a request of approximately $70 million that will be required. This has not been reviewed at the OMB level. They only received our request on September 15. So that really is my request which is under review.

Senator WEICKER. Let me just indicate to you as soon as you can get the final product into our hands, we will move. It would sound to me like probably that is not going to be in time for the markup next Tuesday. On the other hand, it will probably be another week that goes by before we get to the floor. I will be glad to, if need be, amend it on the floor. I thank you for your testimony. Whatever you ask for, you are going to get.

I am also glad, especially, to see the review process goes on continually among yourselves. Indeed, this has been the nature of the process between the executive and the congressional branches.

Dr. MASON. Thank you, and we will try to provide that information.

Senator WEICKER. How do you care to proceed? Do you have a batting order here?

Dr. MASON. We can go as it is on your schedule. I don't have that in front of me now.

Senator WEICKER. We will have as our next witness Dr. James Wyngaarden, Director of the National Institutes of Health. Please proceed. I am going to save, Senator D'Amato, all questions until the end.

STATEMENT OF JAMES WYNGAARDEN

Dr. WYNGAARDEN. Thank you, Mr. Chairman. I am pleased to provide the committee with an overview of ongoing activities and research objectives of the National Institutes of Health on acquired immunodeficiency syndrome. Although tremendous progress has been made, much remains to be learned concerning the treatment of AIDS patients and the ultimate prevention of this deadly disease.

NIH has maintained a strong and growing research effort prior to and since the first AIDS patients were admitted to the NIH Clinical Center more than 4 years ago.

As you pointed out, Mr. Chairman, it was this backlog of investments in biology knowledge that allowed us to make such rapid progress in this disease. We are committed to determining the frequency and distribution of AIDS in the population, its mode of transmission, and the means for treatment and prevention of the disease.

We recognize that AIDS research and its associated planning must be a dynamic process punctuated by new discoveries and the inevitable adjustments that these developments impose. The NIH planning and budget processes allow the flexibility needed to redirect our focus and best utilize our resources.

To assure that NIH would be prepared to respond rapidly and be fully informed of all AIDS activities, the NIH working group on AIDS was established in 1982 to coordinate and exchange information among the bureaus, institutes, and divisions of NIH, as well as with the Alcohol, Drug Abuse, and Mental Health Administration, the Centers for Disease Control, and the Food and Drug Administration. This high level of collaboration was enhanced by the creation by the Assistant Secretary for Health of the PHS AIDS executive task force to expedite the large-scale practical applications of AIDS and AIDS-related findings.

The NIH working group was replaced by the NIH AIDS executive committee in June 1984. The purpose of the NIH AIDS executive committee is to keep the NIH Director fully informed on AIDS and AIDS-related matters. The committee also provides a mechanism to heighten coordination among elements of NIH so that all new research opportunities are fully exploited and explored.

As the need arises, the NIH AIDS executive committee establishes subcommittees to address specific problems, such as the subcommittee for the development and testing of prophylactic and therapeutic modalities for the control of AIDS and the subcommittee for the development of appropriate animal models.

Senator WEICKER. Dr. Wyngaarden, will you pull the microphone a little closer to you, please?

Dr. WYNGAARDEN. Current research supported and conducted by NIH includes studies of the chemistry and biology of the causative virus itself, basic studies supporting the development of reliable diagnostic tests for AIDS; epidemiologic studies, including examination of cofactors that might play a role along with HTLV–III in causing AIDS; work aimed at reconstituting the immune system in AIDS patients; inhibiting and eradicating the retrovirus HTLV–III with antiviral agents and controlling the opportunistic infections and cancers characteristic of the disease; also, application of several techniques to the development of vaccines, including the search for animal models for AIDS; and studies aimed at more effective screening of donated blood.

Special emphasis is being given to drug research and testing in the treatment of AIDS. It is likely that patients will have to be treated with at least two agents simultaneously, an antiviral agent and an immune enhancer, in order to successfully combat the disease. However, more research is needed to answer this point definitively. Antiviral agents identified as having clinical potential are currently being tested or are in preparation for testing. Studies must first be done to ensure these drugs are generally safe and will not further compromise the weakened state of the patient with AIDS.

In regard to vaccine development, NIH researchers working in close cooperation with colleagues at the FDA are currently investigating a number of preparations by breaking up the whole AIDS virus and extracting antigens. These preparations are now being tested in animals for evaluation of their effectiveness as a potential vaccine.

Additionally, a number of NIH investigators are using recombinant DNA technology in an attempt to clone appropriate segments of HTLV-III.

The rapid progress that has been made thus far in AIDS research is due in large part to the extensive and farsighted previous investments in basic science, particularly in the areas of immunology and virology. Of course, there is still much to be learned about the virology and pathogenicity of the virus. Therefore, the institutes will continue to actively support basic research involving antigenic viral components, stressing antigens that are common to many virus strains and would elicit neutralizing and/or protective antibodies, as well as other studies on isolation from body fluids; identification of markers for predicting occurrence of the disease.

A wide range of epidemiologic research on AIDS is being conducted at NIH, by its grantees and in collaboration with other agencies of the PHS. The objectives of these studies are to develop an understanding of how infection occurs, how frequently and under what circumstances HTLV-III infection persists in infected individuals and which infected individuals are most likely to transmit HTLV-III; the severity of the disease in relation to time and source of infection; risk factors; timeframes for the development of antibodies to HTLV-III; and the role of host factors and cofactors in disease risk.

Examples of work in this area include: Studies in various populations to assess the prevalence of HTLV-III infection by using the HTLV-III antibody ELISA test and viral isolation. Groups being examined include homosexual men, hemophiliacs, drug users, family contacts, hospital and laboratory personnel, blood donors, and several populations in the United States and in Haiti, Central Africa, and the Far East.

The studies include support of a large multicenter study of the natural history of AIDS in homosexual men. Specifically, 5,000 homosexual men in Baltimore, San Francisco, Chicago, Los Angeles, and Pittsburgh are being followed longitudinally for 3 years.

The objective is to resolve issues concerning the clinical spectrum of HTLV-III infections for an individual, the prevalence of circulating and/or shed virus in antibody positive persons, and the prognosis for seropositive individuals with mild or no signs of disease.

There is also a large study of the natural history of HTLV-III infection in newborn children. This involves the identification of HTLV-III positive pregnant women, spouses of patients, parenteral drug users and Haitians, and the subsequent laboratory and clinical evaluation of their offspring up to 2 years of age.

Other studies involve the treatment of AIDS-associated ocular infections. And a study of HTLV-III transmission in seropositive, pregnant, drug-using females and their offspring, with followup of the children to monitor seroconversion, immune function, and risk of AIDS.

There is also a study with clinical centers in New York, San Francisco, Miami, Los Angeles, Detroit, and Seattle to determine the incidence and natural history of HTLV-III infection. The study will include 1,000 hemophiliacs, 100 persons with sickle cell disease, and about 150 with Cooley's anemia. The results of the study will be important to understanding the role and relative risk of various types of blood components in transmission of HTLV-III.

Additionally, there is a study of the collection of serum samples from randomly selected volunteer blood donors at major blood centers in New York, San Francisco, Miami, and Los Angeles prior to the development of the HTLV-III test. This serum repository will be used for testing antibodies to HTLV-III, identification of seropositive donors and recipients of blood products from these donors, followup of the recipients, and data analysis.

Further studies are related to AIDS encephalopathy and the substantial data that the retrovirus HTLV-III is present in the brain of AIDS patients.

The objectives of studies related to treatment are the development and evaluation of antivirals and immune stimulants, as well as combinations of these which are effective against AIDS. Research objectives being pursued in close collaboration with FDA in this critical area will include:

Immediate investigation of the safety and efficacy of HPA-23, made possible by the recent review of an investigational new drug application by the FDA.

In addition, there are phase I studies of other antivirals and immune modulators, which are being done in our intramural programs. Some of these studies involve interleukin-2, ribavirin, foscarnet, and suramin. Agents having a tolerable toxicity level at dosages that show some stimulation of the immune system or are active against the AIDS virus will then move on to phase II studies.

Phase II studies are basically an extension of phase I studies, involving larger numbers of patients, to determine the effective dosages. If these studies are successful, controlled efficacy trials, phase III studies, will follow.

Of the agents under review, suramin continues to be viewed as a promising drug, as there is strong evidence that it has clinical activity against HTLV-III. To date, a number of patients are involved in trials with this drug, and more trials are planned with larger numbers of patients.

Clinical trials with ribavirin and related drugs are ongoing in the treatment of pediatric AIDS patients. In phase I, promising antiviral agents will be tested for their efficacy in eliminating viremia. Serum and cerebrospinal fluid levels of virus will be evaluated against dosage and toxicity.

NIH is working closely with agencies throughout the PHS in developing improved methods for detection and control of this disease. The principal objectives of NIH efforts in the prevention area are to develop and evaluate better approaches for detecting infection as well as to develop passive and active immunoprophylaxis. A variety of activities will be undertaken in the prevention area. These include improved methodology to detect AIDS antibody; attempts to develop methodologies for early detection of disease; and simple, rapid, and sensitive methods for the detection and isolation of the HTLV-III virus.

A great many methods of vaccine production will be considered. These will include extracting candidate antigens from large-scale production of virus, identifying appropriate antigens and synthesizing them, insertion of appropriate genomes in bacteria or yeast for antigen production, insertion of appropriate HTLV-III genome segments into vector viruses and synthesis of peptides of the viral envelope products.

When candidate vaccine materials have been shown safe and antigenic in animals, phase I clinical studies will begin in humans.

Hyperimmune serum and monoclonal antibodies will be developed to determine their feasibility in the treatment of AIDS and/or AIDS-related complex.

We also have ongoing studies in the development of animal models. The objective of these studies is to continue to develop animal models of AIDS in which candidate vaccines and drugs can be tested.

Information programs have been designed to promote a fuller understanding of AIDS and to disseminate the latest research advances to those involved in the care of AIDS patients. For example, a series of workshops, seminars and conferences, and outreach education programs has been held aimed at different populations, including physicians, health care workers, allied service personnel dealing with AIDS patients, and lay individuals. As an example, NIAID has developed an Outreach/Technology Transfer Program specifically designed for health workers and allied support personnel who care for AIDS patients. These conferences have been held in a number of U.S. cities, and the program will continue. The purpose of these conferences is to provide the most recent information and to dispel myths and fallacies regarding AIDS.

There is current support by the National Heart, Lung, and Blood Institute to identify the most effective methods to inform and counsel blood donors who are identified as HTLV-III antibody positive, and that will continue.

Use of the physician's data query system, or PDQ, developed by the National Cancer Institute as a means for providing physicians with information about standard and experimental treatment of cancer, locations of experimental treatment, and the names of cancer specialists, to respond to the AIDS crisis and make the most recent information on AIDS available to health practitioners. NCI has included information on ongoing AIDS studies in the PDQ system, and it will have a complete register by January 1986.

Also, information support is being provided by the National Library of Medicine through bibliographic and reference services. NLM is producing a comprehensive bibliography on AIDS, which will be available both to the Department and to extramural AIDS investigators.

In summary, Mr. Chairman, I believe I have provided the committee with an overview of NIH activities that demonstrate our major commitment toward developing treatments, a vaccine and ultimately a cure for AIDS. The fast pace of AIDS research at NIH and in the numerous research institutions in this country and around the world makes almost any research planning effort dated before it is complete.

NIH research efforts directed toward the AIDS problem are both logical and comprehensive. Our efforts, fully coordinated with other agencies of the PHS, are broad and multifaceted, since no one can predict which approach will ultimately be successful. We all hope for new findings in this area, and are prepared to apply those results to our research effort upon discovery.

This concludes my summary, Mr. Chairman. I will be pleased to answer any questions you may have.

Senator WEICKER. Before moving to the next witness, which will be Donald Hopkins, Acting Director for the Centers for Disease Control, the purpose of these hearings, aside from gaining the knowledge that the committee needs in order to make its appropriations, is to also communicate the best scientific knowledge to the American people.

As I indicated before, I can speak as to what the Appropriations Committee has done, is doing or will do. That I am knowledgeable about, but like many others, when we get into the area of science, I am listening, not talking or asking. I would like to afford the opportunity, since we have not only the individuals I have introduced, but I also see my good friends Dr. Lenfant of the National Heart, Lung, and Blood Institute; Dr. Fauci of the National Institute of Allergy and Infectious Diseases; and Dr. DeVita of the National Cancer Institute. They are all here in this room.

If there are members of the public or press present that have questions that they would like to submit through the chair in order to clarify what sometimes gets to be highly technical or scientific explanations, I would be more than glad to afford them the opportunity to do just that. So if there are those questions that one seeks an answer to through the chair, then submit those questions to Pat Falsey over here of the staff. I will see to it as best I can that those questions are asked.

In the absence of that, not desiring to do that, I will ask the public and press present if they do have questions, these individuals will be in the room, they will be available to go ahead and talk to you. I think this is terribly important as a result of this hearing that the facts get out and the speculation stop and the sooner it stops and the sooner they are placed on a basis of facts, the easier it will make the task of these gentlemen and their colleagues in the scientific field.

Our next witness will be Dr. Hopkins. It is a pleasure to have you here, Dr. Hopkins.

STATEMENT OF DONALD R. HOPKINS

Dr. HOPKINS. Thank you, Mr. Chairman. I am pleased to appear before you today to discuss CDC's activities in prevention and control during fiscal year 1985 and our proposed activities in fiscal year 1986.

When clusters of a rare cancer, Kaposi's sarcoma and pneumocystis carinii pneumonia were first recognized in homosexual men in 1981, CDC took a lead role in investigating these disturbing phenomena. As a result of early epidemiologic investigations and in an effort to standardize reporting, we developed a case definition which was to become known later as AIDS.

A nationwide surveillance program was established to monitor trends as the epidemic progressed and specialized epidemiologic studies were initiated to investigate modes of transmission and to identify those factors and groups associated with increased risk of developing AIDS.

Surveillance studies showed very early that AIDS was spreading rapidly in certain populations and that the disease would soon become a major public health concern. One important surveillance tool early in the AIDS epidemic was an increasing demand on the CDC Drug Service Program for distribution of pentamidine isothionate, a drug used in the treatment of pneumocystis carinii pneumonia. Pneumocystis is an infection most commonly seen in immunocompromised patients. CDC had started distribution of pentamidine isothionate to treat pneumocystis under an IND license in 1967. An increase in requests for this drug was noted in 1981 and by 1984, more than 350 patient doses were distributed each month, a clear indication of the increasing number of AIDS cases in this country. Because of increasing demand for this drug to treat AIDS patients, CDC and the FDA actively sought a U.S. producer and possible distributor for pentamidine in 1983. In November 1984, CDC discontinued distribution of pentamidine after the drug became commercially available.

Epidemiologic studies and investigations into individual cases by CDC defined certain populations at high risk for AIDS. These included sexually active homosexual and bisexual males, IV drug abusers, and recipients of blood and blood products, especially patients with hemophilia.

These findings strongly suggested that a blood-borne agent, probably a virus, was responsible for the disease. Laboratory studies identified imbalances in patients' immune systems, indicating that the white blood cells, responsible for defending the body against the disease, were being destroyed.

In order to speed research into this new disease, CDC became a major center for disseminating information rapidly. As you heard, as of today, we have put 64 articles thus far in the "Morbidity and Mortality Weekly Report." Controlling the spread of AIDS also required assertive action at the State and local levels. Therefore, CDC collaborated with State and local health departments and other community groups whose organized participation was essential for success.

Much of CDC's resources to date have been directed toward those States and communities with the highest incidence of AIDS. Collaborative efforts have been designed to enhance communitywide surveillance for AIDS, to protect the Nation's blood supply through the provision of alternate test sites and to stimulate health education and risk reduction activities.

We have also worked closely with a number of States and communities on epidemiologic research to answer some of the fundamental questions of concern.

During fiscal year 1985, CDC has expanded AIDS surveillance, epidemiologic studies, and laboratory investigations and has initiated major health education and risk reduction activity. Our total appropriation in fiscal year 1985 for these activities, which I will discuss in more detail below, has been $33.2 million.

National surveillance of AIDS has been maintained and upgraded through mathematical modeling of current and future trends. The completeness of case reporting is being verified in several States and cities and patients surviving over 3 years are being epidemiologically characterized.

Cooperative agreements are providing financial and technical assistance to 23 State and major city health departments for active AIDS surveillance.

Current epidemiologic studies include investigation of blood donors in transfusion acquired AIDS cases, study of families of hemophiliacs and other AIDS victims, intensive investigation of patients outside the usual high-risk groups, studies of transmission in Central Africa, and studies of health care workers who have had inadvertent needle-stick injuries.

One of these studies is following a cohort of 7,000 homosexual men in San Francisco to determine the incidence, risk factors, and natural history of AIDS disease and infection. We are performing a number of studies to determine risk factors and determine spread in homosexual or bisexual men. Laboratory support for these studies have also been provided, included characterization of the immune response to HTLV-III/LAV infection. We have determined the susceptibility of the virus to various disinfectants and are actively searching for an animal model of HTLV-III/LAV infection.

In anticipation of FDA's licensure of a serologic test for antibodies to HTLV-III in March, CDC conducted 44 1-day seminars in 34 cities on antibody testing for this virus during February 1985. These seminars brought information about the test and its interpretations to over 7,500 health workers.

CDC followed these seminars by spending $10.4 million to help implement alternate site testing in the States. These sites were intended to help protect the Nation's blood supply by providing an alternative to blood banks and plasma centers for those persons wishing to know if they had been infected by HTLV-III. We also assisted health officials in producing a guide on management of alternative site testing. At present, HTLV-III antibody testing is available in 518 alternative sites in 52 States and territories. This initiative has served its mission to help protect the Nation's blood supply. .

We also have been operating a national hotline which answers more than 700 calls daily from the general public on AIDS and makes appropriate referrals for further information. We are about to award $1.2

million in cooperative agreements to demonstrate the impact of current health education and risk reduction methods and to test innovative approaches to prevent the spread of AIDS.

CDC continued a cooperative agreement with the U.S. Conference of Mayors to help fund grassroots AIDS health education and risk reduction efforts of 19 community based organizations.

We also funded a study of the nature, scope, and evaluability of AIDS health education and risk reduction efforts conducted to date in nine large cities.

The President's fiscal year 1986 budget request asks for $45.6 million for AIDS activities at CDC. This request includes an amendment for $26.925 million. With these funds, CDC will continue and expand many critical activities initiated in fiscal year 1985, in accordance with the Public Health Service's plan for the prevention and control of AIDS. That plan calls for continuing to clarify the epidemiology and natural history of the HTLV-III infection and AIDS, continuing to implement national and community risk reduction and information programs as early prevention measures, designing and evaluating improved prevention and control measures, and designing and promoting prevention and control programs that grow in effectiveness through incorporation of new intervention tools, such as vaccine and antivirals, as they become available.

Particular attention will be paid in fiscal year 1986 to the role of heterosexual transmission and other aspects.

Approximately $2.4 million will be used in fiscal year 1986 to expand our surveillance activities. We will attempt to define the magnitude and trend of infection and disease in several special groups and geographic areas. Laboratory proficiency for HTLV-III testing in States and local laboratories will be examined. CDC also plans to use $3.825 million to expand epidemiologic studies to determine the role of specific sexual practices and other potential risks or protective factors influencing heterosexual transmission; compare frequency of sexual transmission from female to male with that from male to female; document the prevalence of infection in prostitutes and correlate these findings with history of IV drug usage and other factors; to continue to evaluate the risk of spread in day care centers and hospitals and study the spread of the virus among households in Zaire to clarify risk factors for transmission among spouses, siblings, parents, and children living in households of infected persons. Results from these studies are expected within the next 1 to 3 years.

Until a vaccine and/or therapy for AIDS is developed, the only prevention program available is health education/risk reduction. The budget amendment includes $20.7 million to reduce transmission through education which is aimed at encouraging high-risk individuals to change related aspects of their behavior.

CDC plans to spend $5.4 million to assist States in building a core capacity directed toward the prevention of AIDS and the transmission of the infection. When new scientific findings and health education/risk reduction approaches are developed, the States would then have the systems in place to rapidly disseminate the new prevention strategy.

In addition, 15 of the highest morbidity areas will receive approximately $7.8 million to intensify their prevention efforts and implement evaluation mechanisms to monitor their effectiveness.

To determine the most effective health education/risk reduction programs and techniques, demonstration and evaluation projects will be funded for approximately $4.2 million in three or four States and cities to support intensive projects for prevention of AIDS and HTLV-III/LAV infection. The evaluation of the effectiveness of the educational programs will be accomplished through surveys to document changes in the understanding of the AIDS risk factors and to evaluate changes in risk-associated behavior and infection rates resulting from program efforts.

Trends will also be monitored in other illnesses which are sensitive indicators of behavior change in high-risk populations. Information gained from these demonstrations will be shared promptly with all States to increase the cost effectiveness of their ongoing activities.

To stimulate new approaches to community health education/risk reduction programs, we also will award about $2 million to encourage unique and innovative approaches to prevent and/or control transmission. Approximately 10 projects would be supported in the community organizations, public health departments, and other organizations.

Finally, included in the requested amendment is $1.265 million for technical assistance to States to help them improve program effectiveness and reduce costs. This assistance will include national strategy planning, refinement of risk reduction guidelines; development of demonstration and evaluation projects; development of uniform evaluation guidelines and instruments; expanded support of the hotline and provision of training to health department and community personnel.

It is clear that AIDS continues to be the Nation's highest public health priority. In the absence of an effective treatment or vaccine, we intend to do all we can in the areas of surveillance, epidemiology, and health education in order to reduce the transmission of this virus.

This concludes my statement, Mr. Chairman. At the appropriate time, I will be glad to help answer any questions you have.

Senator WEICKER. The next witness is Dr. Donald Macdonald, Administrator of the Alcohol, Drug Abuse, and Mental Health Administration.

STATEMENT OF DR. DONALD MACDONALD

Dr. MACDONALD. I am pleased to be here today to discuss the role of the Alcohol, Drug Abuse, and Mental Health Administration in the Department's efforts with AIDS. ADAMHA is vitally involved with PHS efforts to prevent and control AIDS. As Dr. Mason has indicated, although the major risk groups for AIDS are homosexual and bisexual men, approximately 17 percent of all AIDS patients are intravenous drug users. In addition, another 8 percent are both IV drug users or gay or bisexual men. Psychosocial consequences are common for both the AIDS patient as well as for those with known HTLV–III infection, the causative agent for AIDS. More than 50 percent of AIDS patients develop dementia and/or psychosis during the course of their illness and one in five of these demonstrate neurocognitive and behavioral change before the diagnosis of AIDS is confirmed. These clinical observations are presumed secondary to a direct viral infection of the brain with HTLV–III virus.

As part of the PHS effort to prevent and control AIDS, ADAMHA will focus activities in three areas: one, epidemiologic investigations; two, prevention and control recommendations; and three, risk reduction programs. We will collaborate with NIH and CDC in efforts to monitor the incidence of AIDS, to establish the diagnostic criteria for AIDS, and to maintain surveillance of AIDS-related complex, ARC. We are also preparing AIDS information relevant to the psychosocial aspects of AIDS and the drug use aspects of AIDS.

In addition, the agency strategy and implementation plans to prevent and to control AIDS include: preparation of educational and information materials which we are going to direct to drug abusers and to health care personnel caring for them; preparation of a monograph directed toward the health care worker addressing the psychosocial needs of AIDS patients and persons infected with HTLV–III; and research into epidemiologic and neurobehavioral aspects of AIDS. To date, ADAMHA has provided support for research on AIDS totaling $6.5 million. Utilizing these funds we have looked at the prediction or sexual behavior change in high-risk groups, performed epidemiologic studies of AIDS among IV drug users, psychoimmunologic correlates of AIDS, and studied interactions between psychoactive drugs and their outcome on viral illness. Two ADAMHA institutes are particularly concerned, the National Institute on Drug Abuse [NIDA] and the National Institute of Mental Health [NIMH], both of which have primary roles in our AIDS activities.

NIDA's current efforts are directed toward assessing the spread of HTLV–III exposure, AIDS and AIDS-related complex among the drug using population, and addressing the needs of the drug users already infected by the virus or symptomatic of AIDS. The Institute's activities have focused on three principal populations: those drug users currently infected; other drug users at high risk and concerned about the disease, and drug abuse treatment and service providers. We are concerned about developing more effective prevention measures to incorporate the increased knowledge about this disease and assist in stopping the spread of AIDS in these populations.

To accomplish these goals, NIDA intends to continue its ongoing prevention activities and information dissemination efforts.

Specifically, NIDA works in a number of areas. The first is reducing IV drug use, which is part of NIDA's principal mission, the reduction or elimination of drug use. Because of the AIDS problem among IV drug abusers, this mission becomes more important and reducing drug use will, obviously, decrease the spread of AIDS.

Second, NIDA is attempting to clarify the epidemiology and natural history of drug users. Studies have examined samples in both high and low prevalence areas for AIDS in the drug user population. Studies of the interaction of drugs and their abuse with human function hold great possibilities for clarifying the cofactors.

NIDA also stimulates and conducts research and development of effective prevention approaches and treatment agents. NIDA efforts center on research related to HTLV-III disease among the drug using population. In addition to the epidemiologic studies, we are looking at intervention strategies to determine their efficacy in reducing the spread of HTLV-III disease among the drug-using population.

NIDA is working with national, State, and community risk prevention and education programs to enhance prevention and control measures. We continue to develop and disseminate information aimed at reducing the incidence of HTLV-III and to disseminate information to specific high risk groups and to the general public about the relationship among drug abuse, the spread of HTLV-III, and the subsequent development of AIDS and AIDS-related complex.

NIDA designs and evaluates improved prevention and control measures. One aim is to expand our knowledge base for transfer and technical assistance activities aimed at better informing drug abuse treatment providers about methods and procedures most suited for serving drug abuse clients infected with or at risk of becoming infected with the AIDS virus.

Efforts are aimed at engaging in drug abuse treatment, and other appropriate medical programs, drug users who have AIDS or other stages of infection or who are at high risk of contracting or spreading HTLV-III. Because there are significant geographic differences in the incidence of AIDS among IV drug users, control programs recommended may vary from State to State.

The National Institute of Mental Health's [NIMH] current efforts are directed toward understanding the psychiatric, behavioral, and psychosocial aspects of AIDS. This includes identifying those psychological and behavioral factors which may negatively or positively influence the course of illness and identifying the relationship between immune function and mental health status, such as depression, anxiety, or responses to high levels of stress. Specific activities are in the area of research and support services. We are supporting investigations focused on psychiatric, biobehavioral, neuropsychologic, and psychosocial aspects of AIDS.

Investigators supported by the Institute are developing neuropsychologic instruments specific to AIDS patients; identifying those factors predictive of sexual behavior change associated with the AIDS epidemic; delineating the different psychologic responses of the AIDS, ARC, and HTLV-III patients; and studying the cognitive change associated with and antecedant to the development of AIDS.

NIMH also participates in the implementation of national, State, and community risk prevention and education programs. We are continuing to develop information on the mental health consequences of AIDS directing our research and dissemination efforts toward several specific groups, including health care providers, care givers, and community-based AIDS organizations. This information includes knowledge of the psychological and psychosocial issues related to the high risk groups, those in contact with AIDS patients, and those with AIDS or AIDS-related complex as well as the medical/psychiatric complication of HTLV-III and their clinical manifestations, such as delirium and dementia. These dissemination activities continue to be conducted through a variety of mechanisms including the press and other media, and utilizing national professional association contacts and efforts to work with local radio and television.

Mr. Chairman, this concludes my formal statement. I would be pleased to answer any questions you might have.

Senator WEICKER. Next witness, Dr. Frank Young, Commissioner of the Food and Drug Administration.

STATEMENT OF DR. FRANK YOUNG

Dr. YOUNG. Mr. Chairman, I would like to submit my full statement for the record. In order to have more time for questions, I will just summarize briefly the major points in the testimony of FDA.

The FDA plays a very important and supportive role in the study of AIDS. Our primary responsibilities are the approval of drugs and devices, assurance of the safety and effectiveness of the blood and plasma supply, and virology and vaccine studies with scientists at NIH and CDC. Perhaps the best indication of the type of successful public and private partnership that has occurred for this particular and most dreaded disease is the development of the blood screening test for HTLV-III antibody.

In this sense, in less than 1 year from the isolation of the virus, we had in collaboration with NIH the ability for the mass production of the virus, and with the efforts of the Secretary to secure interaction with the private sector, applications were let for licenses for this test. In less than 1 year, the blood test was able to be approved and it is now implemented widely in blood banks and plasma centers. That could only occur if there was a rapid sharing of information and a deep cooperation between the research scientists in the National Institutes of Health, the academic community, and those within the private sector.

FDA will continue to pledge this type of cooperation in meeting the crisis in AIDS which we view as the most significant public health problem facing the Nation today.

In regard to the issues dealing with therapy, much has already been developed in the previous testimony. I will only highlight a few issues. Of the drugs that are currently in clinical trials in AIDS patients, there are yet not sufficient data to establish their effectiveness in the treatment of AIDS. There are a few compounds, many of which were mentioned by Dr. Wyngaarden, for which there is some preliminary clinical evidence of possible usefulness in the treatment of AIDS or opportunistic infections. I must point out, however, a number of the antiviral drugs may have significant toxicity. In the case of immune modulator symptoms there is a danger of providing enhancement to viral replication and shortening the time of the disease progression so that we must study these very carefully to be sure of the side effects.

We go through a very careful phase I study of investigation of new drugs and then in expanded clinical trials in phase II and phase III.

Despite these complexities of clinical investigations in a disease in which the natural history is not entirely understood, we are prepared to review expeditiously all investigational and marketing applications for products for AIDS, AIDS-related complex and opportunistic infections as we have for HPA-23 and are now doing for the recently filed new drug application for isoprinosine. It is our goal to have what Dr. Harry Meyer calls a zero timing IND. We will work with the private sector during the development of these new drugs and, as expeditiously as we possibly can, turn these applications around.

I am pleased to tell you the first two that we did under this mode were approved in less than 1 week, as far as investigations of new drugs.

I also wish to stress that we remain most concerned about facilitating the availability of any product that appears to be useful in treating AIDS victims and alleviating the suffering it causes, and we are prepared to work with anyone willing to sponsor clinical investigations consistent with our obligation to safeguard patients used as research subjects.

Similarly, we will be working with NIH in related areas of vaccine development. Here the development of animal models capable of measuring the immunogenicity of the HTLV-III component proteins is most important. Skilled virus research teams in FDA will collaborate with NIH and CDC in the development of such vaccines. Thus, it is important to emphasize the integration of FDA into the total AIDS effort of PHS which has been important in developing the HTLV-III antibody test in the past and the excellent leadership of Dr. Mason coordinating the entire PHS effort which will be extremely important in the future.

I appreciate this opportunity to discuss this before this committee. As you know, FDA falls under the jurisdiction of the Appropriations Subcommittee on Agriculture and Related Agencies in the Senate and the House. Fortunately, these subcommittees and their chairmen have been extremely responsible and responsive whenever we have come to them with requests for funds urgently needed to cope with significant public health problems. In fact, Mr. Whitten personally sponsored a floor amendment to include an additional $2,145,000 to support other additional AIDS activities for FDA in fiscal year 1986. This amendment was passed and these resources were included in the appropriation act passed by the House on July 24. I am also pleased to report this amount was included in a bill reported out of the Senate Appropriations Committee on September 24.

Let me briefly discuss with you our plans to utilize these resources in 1986. During the past 12 months, several major developments relevant to transmission, prevention, and control of HTLV–III infection and AIDS have occurred. Serologic tests to detect HTLV–III antibodies have been licensed, and tests are being used to screen donated blood and plasma. Furthermore, a number of therapeutic products have entered into clinical trials and are under active investigation. Our resources will be used to expedite the approval of IND's and the approval of new drug applications so we can bring to the market as fast as it is safe and reasonable, new therapeutic agents to aid those most critically ill and suffering victims and, most importantly, to aid in the prevention of this disease.

The pace of these developments requires that FDA expand surveillance and monitoring efforts. Activities undertaken as part of this request will increase our knowledge regarding the screening test to enhance our ability to assure the safety of the Nation's blood supply and expand the capacity for review and approval of new diagnostic and treatment products.

Additionally, we communicate frequently with the physicians in the country and with health professionals with our drug bulletin. I would like to submit for the record the recent "Dear Doctor" letter I sent out to 175,000 physicians in the country and the upcoming FDA bulletin, if I could, sir, to provide additional information for the record.

Senator WEICKER. Without objection, they will be placed in the record at this point.

[The information follows:]

DEAR DOCTOR LETTER

Dear Doctor:

The Public Health Service (PHS) recently published provisional recommendations for screening donated blood and plasma for antibodies to the HTLV-III virus which causes the acquired immunodeficiency syndrome (AIDS). A copy of those recommendations is attached to this letter for your information, and I strongly suggest that you keep this letter and the attachments on file for future reference. Test kits using the ELISA* technology for detecting HTLV-III antibodies will soon be licensed by FDA and will be commercially available. Blood and plasma collecting facilities will begin testing soon thereafter. Although this is NOT a test for AIDS, there will be individual donors who are found to be reactive in a test for antibodies to the HTLV-III virus and, as suggested in the PHS recommendation, those donors will be referred to a physician for further evaluation. The purpose of this letter is to alert you to the possibility that one or more such donors may be referred to you, and to provide you with as much information as we currently have on how to evaluate such an individual. Based on preliminary information, we expect that less than 1 percent of donors will be reactive for HTLV-III antibodies after repeat testing at the blood or plasma collecting facility. Reactive HTLV-III tests may be due to subclinical infection, to immunity, to an active carrier state, or may represent biologically false-positive reactions such as cross-reactivity to antigens or other viruses. We do not yet know how many blood and plasma donors will fall into each category.

Additional PHS suggestions for the medical evaluation of referred donors are included with this letter. You will also find a sample information sheet which will serve as a model to educate donors at blood and plasma collecting facilities about the antibody test and a sample information sheet for donors with a positive antibody test.

The PHS has placed a very high priority on expediting the development and approval of the HTLV-III antibody test so that it could be used to screen blood and plasma prior to use. Used in that context, the test achieves an important public health goal. However, it is vital that both physicians and patients understand that the antibody test is NOT a test for AIDS. As with any serologic test, there will be some false-positive results, even in samples which are repeatably reactive. When true HTLV-III antibody is present in an otherwise asymptomatic individual, it could mean that infection with the virus has occurred without any clinical evidence of disease. Limited observations indicate that only a small proportion of those individuals will go on to develop AIDS. The natural history of HTLV-III infection is not completely understood at present, and it is not possible to identify by laboratory or other means those asymptomatic persons with antibody to HTLV-III who will eventually develop AIDS. Therefore your clinical judgement is the most important aspect of the evaluation of individuals with antibody to HTLV-III, especially since the test is primarily designed to screen blood and plasma.

Whenever there is a reactive test for antibody to HTLV-III in blood and plasma donors, the PHS recommends that additional serologic testing be considered to clarify the significance of the screening test results. The Western blot* technique has been the most extensively used test for HTLV-III antibody specificity in the research setting. Based on data available to date, minimal criteria that define a positive Western blot test have been established by the PHS, as described in the attached Provisional Recommendations. Western blot testing will be available through most of the manufacturers of the antibody test kits. Further information about the availability of Western blot testing can be obtained through your local blood bank. You may also be able to get additional information through your State Health Department. It is important to recognize, however, that the Western blot test is still considered a research tool which has not yet been fully standardized. Furthermore, when the HTLV-III screening test is positive, negative Western blot result does not necessarily mean that antibody specific to HTLV-III is absent because the relative sensitivity of each of the tests varies among laboratories. In addition to blood or plasma donors who might be referred to you as the result of a reactive screening test for HTLV-III antibody other patients may ask you to determine their HTLV-III antibody status because of concern that they may be at risk of developing AIDS. Such individuals should be given information about the implications of the ELISA test BEFORE being tested, with particular emphasis on the significance of a positive result. In addition, physicians and other health professionals should recognize the need for assuring the confidentiality of test results because disclosure could lead to serious social and employment consequences. Loss of employment or insurability may occur if positive test results become a part of the medical record.

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*ELISA is an acronym for enzyme-linked immunosorbent assay. This assay utilized the principle of a solid phase (e.g., beads or microtiter plate wells) coated with antigen or antibody and an indicator reagent, antibody or antigen, respectively, to which an enzyme has been conjugated or "linked".

A typical ELISA test such as that used for the detection of antibody to HTLV-III utilizes beads or microtiter wells coated with disrupted, inactivated HTLV-III virus antigens and goat anti-human Ig conjugated or "linked" to an enzyme which on incubation with the appropriate substance will produce a color.

When an unknown serum or plasma sample is tested for the presence of antibodies, it is placed in the antigen-coated wells; the antibody in the sample links to the antigen on the solid-phase carrier and is detected by the anti-human antibodies conjugated to the enzyme.

Because, as noted above, the natural history of the disease is not completely understood at the present time, the medical significance of a positive result is unknown in terms of its predictive value for an asymptomatic individual. Furthermore, there may be biologically false-positive reactions due to cross-reactivity to antigens of other viruses. Individuals who seek testing should also recognize that a negative antibody test result does not necessarily mean that they are free of virus. Antibody may not have developed, or be undetectable, if exposure was recent. There is at least one report that 4 of 96 individuals carried the virus for 6 months without developing detectable antibodies. Because a positive test result can be difficult to interpret for an asymptomatic individual, consideration also should be given to the severe psychological stress which would be placed on the individual if the test for antibody to HTLV-III is positive. Appropriate counseling should be available if HTLV-III testing is done.

As significant new information is developed and new products become available to help in the diagnosis and treatment of AIDS, we will continue to take steps to inform the medical community.

Sincerely yours,

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

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*The term "Western blot" refers to a technique for identifying antibodies to proteins of specific molecular weight. The technique therefore allows the identification of antibodies to specific proteins associated with the HTLV-III virus. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands). In general this test is less sensitive than the ELISA but more specific if positive.

MORBIDITY AND MORTALITY WEEKLY REPORT, JAN. 11, 1985,
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Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome

In March 1983, the U.S. Public Health Service issued inter-agency recommendations on the prevention of acquired immunodeficiency syndrome (AIDS) (*1*). Included was the recommendation that members of groups at increased risk for AIDS should refrain from donating plasma and/or blood. That recommendation was made to decrease the risk of AIDS associated with the administration of blood or blood products, which accounts for about 2% of all reported AIDS cases in the United States.

Evidence has shown that a newly recognized retrovirus is the cause of AIDS. Although this virus has been given several names, including human T-lymphotropic virus type III (HTLV-III) (*2*), lymphadenopathy-associated virus (LAV) (*3*), and AIDS-associated retrovirus (ARV) (*4*), it is referred to as HTLV-III in this discussion. Tests to detect antibody to HTLV-III will be licensed and commercially available in the United States in the near future to screen blood and plasma for laboratory evidence of infection with the virus. The antibody tests are modifications of the enzyme-linked immunosorbent assay (ELISA), which uses antigens derived from whole disrupted HTLV-III (*5*).

There is considerable experience with the ELISA test in research laboratories, but much additional information will be gathered following its widespread application. In the early phases of testing, a number of false-positive tests may be encountered. Adjustments in interpretation are anticipated as more is learned about the performance of the test in an individual laboratory and about the specific proportion of falsely positive or falsely negative tests in the screening setting where the test is used.

The present recommendations concern the use of these tests to screen blood and plasma collected for transfusion or manufactured into other products. They are intended to supplement, rather than replace, the U.S. Food and Drug Administration's recently revised recommendations to blood and plasma collection facilities and the earlier inter-agency recommendations (*1*). Additional public health applications of these tests in the understanding and control of AIDS will be described in a subsequent report.

BACKGROUND

Antibody Detection Studies

The ELISA test has been used in many research programs for detecting antibodies to HTLV-III in patients with AIDS and with AIDS-related conditions. In different studies, HTLV-III antibody was found to range from 68% to 100% of patients with AIDS, and in 84%-100% of persons with related conditions, such as unexplained generalized lymphadenopathy (*5-7*). Serologic surveys have yielded variable seropositivity rates in groups at increased risk for AIDS: 22%-65% of homosexual men (*8-11*), 87% of intravenous-drug abusers admitted to a detoxification program in New York City (*12*), 56%-72% of persons with hemophilia A (*13,14*), and 35% of women who were sexual partners of men with AIDS (*15*). In contrast to the above groups, HTLV-III antibody has been detected in fewer than 1% of persons with no known risks for AIDS (*4-10*).

The time needed to develop a positive antibody test following infection is not known. Data regarding the interval between infection with HTLV-III and seroconversion are limited. A nurse who sustained a needle-stick injury while caring for an AIDS patient developed antibody between 4 and 7 weeks following exposure (*16*). Additionally, a recent study described several asymptomatic individuals infected with HTLV-III for more than 6 months in the absence of detectable antibody (*17,18*). Nonetheless, currently available ELISA tests can be expected to identify most persons with HTLV-III infection.

Virus Isolation Studies

HTLV-III has been isolated from blood, semen, and saliva and has been recovered from many individuals in the presence of antibody (*19,20*). HTLV-III has been isolated from the blood of 85% or more of seropositive individuals with AIDS (*21*), lymphadenopathy, or other AIDS-associated conditions (*2*) and from three of four mothers of infants with AIDS (*2*). The virus has also been isolated from asymptomatic seropositive homosexual men and hemophiliacs, and has been recovered from 95% of seropositive high-risk blood donors who had been implicated in the transmission of AIDS through transfusion (*21*). The recovery of HTLV-III from these high-risk donors 2 or more years after their initial donation provides evidence that viremia may persist for years in both asymptomatic and symptomatic individuals. HTLV-III has also been isolated from some asymptomatic seronegative persons, but this is the exception (*17*).

Modes of Transmission

Epidemiologic data suggest that the virus has been transmitted through intimate sexual contact; sharing contaminated needles; transfusion of whole blood, blood cellular components, plasma, or clotting factor concentrates that have not been heat treated; or from infected mother to child before, at, or shortly after the time of birth. No other products prepared from blood (e.g., immunoglobulin, albumin, plasma protein fraction, hepatitis B vaccine) have been implicated, nor have cases been documented to occur through such common exposures as sharing meals, sneezing or coughing, or other casual contact.

Natural History of Infection

Information about the course of infection with HTLV-III is incomplete, but the majority of infected adults will not acquire clinically apparent AIDS in the first few years after infection. In some studies 5%-19% of seropositive homosexual men developed AIDS within 2-5 years after a previously collected serum sample was retrospectively tested and found to be seropositive. An additional 25% developed generalized lymphadenopathy, oral candidiasis, or other AIDS-associated conditions within the same interval (*11,22*). The long-term prognosis for most persons infected with HTLV-III is unknown.

SCREENING BLOOD AND PLASMA

Initial Testing

Persons accepted as donors should be informed that their blood or plasma will be tested for HTLV-III antibody. Persons not wishing to have their blood or plasma tested must refrain from donation. Donors should be told that they will be notified if their test is positive and that they may be placed on the collection facility's donor deferral list, as is currently practiced with other infectious diseases, and should be informed of the identities of additional deferral lists to which the positive donors may be added.

All blood or plasma should be tested for HTLV-III antibody by ELISA. Any blood or plasma that is positive on initial testing must not be transfused or manufactured into other products capable of transmitting infectious agents.

When the ELISA is used to screen populations in whom the prevalence of HTLV-III infections is low, the proportion of positive results that are falsely positive will be high. Therefore, the ELISA should be repeated on all seropositive specimens before the donor is notified. If the repeat ELISA test is negative, the specimen should be tested by another test.

Other Testing

Other tests have included immunofluorescence and radioimmunoprecipitation assays, but the most extensive experience has been with the Western blot technique (*22*), in which antibodies can be detected to HTLV-III proteins of specific molecular weights. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands).

Notification of Donors

If the repeat ELISA test is positive or if other tests are positive, it is the responsibility of the collection facility to ensure that the donor is notified. The information should be given to the donor by an individual especially aware of the sensitivities involved. At present, the proportion of these seropositive donors who have been infected with HTLV-III is not known. It is, therefore, important to emphasize to the donor that the positive result is a preliminary finding that may not represent true infection. To determine the significance of a positive test, the donor should be referred to a physician for evaluation. The information should be given to the donor in a manner to ensure confidentiality of the results and of the donor's identity.

Maintaining Confidentiality

Physicians, laboratory and nursing personnel, and others should recognize the importance of maintaining confidentiality of positive test results. Disclosure of this information for purposes other than medical or public health could lead to serious consequences for the individual. Screening procedures should be designed with safeguards to protect against unauthorized disclosure. Donors should be given a clear explanation of how information about them will be handled. Facilities should consider developing contingency plans in the event that disclosure is sought through legal process. If donor deferral lists are kept, it is necessary to maintain confidentiality of such lists. Whenever appropriate, as an additional safeguard, donor deferral lists should be general, without indication of the reason for inclusion.

Medical Evaluation

The evaluation might include ELISA testing of a follow-up serum specimen and Western blot testing, if the specimen is positive. Persons who continue to show serologic evidence of HTLV-III infection should be questioned about possible exposure to the virus or possible risk factors for AIDS in the individual or his/her sexual contacts and examined for signs of AIDS or related conditions, such as lymphadenopathy, oral candidiasis, Kaposi's sarcoma, and unexplained weight loss. Additional laboratory studies might include tests for other sexually transmitted diseases, tests of immune function and, where available, tests for the presence of the virus, such as viral culture. Testing for antibodies to HTLV-III in the individual's sexual contacts may also be useful in establishing whether the test results truly represent infection.

RECOMMENDATIONS FOR THE INDIVIDUAL

An individual judged most likely to have an HTLV-III infection should be provided the following information and advice:

1. The prognosis for an individual infected with HTLV-III over the long term is not known. However, data available from studies conducted among homosexual men indicate that most persons will remain infected.
2. Although asymptomatic, these individuals may transmit HTLV-III to others. Regular medical evaluation and follow-up is advised, especially for individuals who develop signs or symptoms suggestive of AIDS.
3. Refrain from donating blood, plasma, body organs, other tissue, or sperm.
4. There is a risk of infecting others by sexual intercourse, sharing of needles and, possibly, exposure of others to saliva through oral-genital contact or intimate kissing. The efficacy of condoms in preventing infection with HTLV-III is unproven, but the consistent use of them may reduce transmission.
5. Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.
6. Women with a seropositive test, or women whose sexual partner is seropositive, are themselves at increased risk of acquiring AIDS. If they become pregnant, their offspring are also at increased risk of acquiring AIDS.
7. After accidents resulting in bleeding, contaminated surfaces should be cleaned with household bleach freshly diluted 1:10 in water.
8. Devices that have punctured the skin, such as hypodermic and acupuncture needles, should be steam sterilized by autoclave before reuse or safely discarded. Whenever possible, disposable needles and equipment should be used.
9. When seeking medical or dental care for intercurrent

illness, these persons should inform those responsible for their care of their positive antibody status so that appropriate evaluation can be undertaken and precautions taken to prevent transmission to others.

10. Testing for HTLV-III antibody should be offered to persons who may have been infected as a result of their contact with seropositive individuals (e.g., sexual partners, persons with whom needles have been shared, infants born to seropositive mothers).

Revised recommendations will be published as additional information becomes available and additional experience is gained with this test.

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AIDS Information for Health Professionals

Clinicians Guide to Evaluation of HTLV-III Antibody Positive Individuals

The Virus that Causes AIDS

The etiologic agent of the acquired immunodeficiency syndrome (AIDS) is human T-cell lymphotropic virus type III (HTLV-III), also known as LAV and ARV. This distinctive class of RNA virus shares some features with retroviruses previously linked to various disorders in animals, including leukemias, neurologic diseases, and immunodeficiency disorders and to a human virus, HTLV-I, linked to an unusual form of human leukemia. HTLV-III has a cytotoxic effect on T-lymphocytes of the helper type. The diverse infections and tumors which are the ultimate cause of death for AIDS patients result from the fact that the virus renders the immune system incompetent.

Clinical Significance of HTLV-III Seropositivity

Over 90% of patients with full-blown AIDS are positive for HTLV-III antibodies in the screening test, and with the application of additional research techniques close to 100% of such individuals are virus-positive. Among seropositive persons, the risk for developing frank AIDS may vary depending upon risk group and possibly other factors such as additional environmental exposures and genetic background. Preliminary estimates in cohorts of homosexual men followed prospectively for two to five years indicate that between 5% and 20% of persons with detectable HTLV-III antibodies may go on to develop AIDS. However, information that pertains to one risk group may not directly translate to other risk groups. The lack of precise data on the clinical significance of HTLV-III antibody positivity for an individual patient coupled with the fact that many persons in high-risk groups have detectable HTLV-III antibodies, creates a dilemma for the physician confronted with evaluating and counseling such antibody-positive patients. If this virus follows patterns seen in other viruses, the majority of exposed individuals will remain clinically healthy. However, this is a new class of human virus and the long-term implications of exposure to the health of an individual are unknown. Furthermore, the implications of seropositivity in the individual to the potential for transmitting the virus to others are unknown. Epidemiologic data do document that homosexual and probably heterosexual sexual relations, needle sharing, blood transfusion and transplacental and/or perinatal exposure are modes of transmission. Finally, it should be emphasized that the current antibody test is licensed as a blood bank screening and not a diagnostic tool. In this regard, the absence of antibody in a high-risk person does not necessarily mean that the patient is virus negative, since the virus has been isolated from a few at-risk individuals who were antibody negative. Conversely, as with all antibody tests of this type, a few biologic false positives will be detected due to antibodies to non-HTLV-III cross-reactive antigens.

Dynamics of HTLV-III Infection

Seroconversion generally antedates the development of clinical or subclinical laboratory signs of viral infection by several years, necessitating extended follow-up. The first sign of subclinical infection may be a laboratory perturbation associated with HTLV-III seropositivity.

The laboratory parameter most frequently linked to HTLV-III infection is a depressed number of peripheral blood lymphocytes bearing the helper T-cell phenotype. Other laboratory parameters which have been associated with this process include elevated immunoglobulin levels; high titers to a variety of viral agents (particularly Epstein Barr virus and cytomegalovirus); and elevated beta-2 microglobulin, thymosin, and acidlabile alpha interferon. Although these various observations are of some research interest and reflect the variety of laboratory perturbations which result from fundamental virus-associated immunodeficiency, their relevance in the clinical setting is not sufficiently well-defined to be of practical diagnostic benefit. These are currently a focus of ongoing research studies.

Range of Clinical Manifestations

Another condition recognized as being associated with HTLV-III infection is the lymphadenopathy syndrome, a medical complex characterized by the occurrence of persistent, unexplained lymph node enlargement in several extra-inguinal lymph node groups. The relationship of the lymphadenopathy syndrome to progression to overt clinical AIDS is uncertain but probably is as high as 10%.

Another lesser manifestation is the AIDS related complex (ARC), a clinical and laboratory syndrome characterized by minor conditions clinically associated with immunosuppression (e.g., oral thrush) and laboratory evidence of immunosuppression. In addition, unexplained idiopathic thrombocytopenia is probably associated with HTLV-III infection, as are a variety of non-life-threatening fungal, viral, and bacterial infectious processes which probably represent manifestations of virus-induced immunologic perturbation. These manifestations are sometimes termed lesser AIDS.

The clinical presentation of clinical AIDS, as originally defined, follows four major patterns:

1) A febrile prodrome of weeks to months followed by opportunistic infection.
2) Abrupt onset of opportunistic infection.
3) Presentation with Kaposi's sarcoma.
4) Progression from the AIDS-related complex.

Approach to Clinical Evaluation

AIDS and its diverse related clinical disorders challenge the diagnostic acumen of physicians in all branches of medicine. The prospective clinical evaluation of HTLV-III seropositive individuals who may be at risk for AIDS requires a careful multisystem approach to evaluate signs and symptoms. Clearly, it is important to take a careful medical and social history and perform thorough physical examinations on these individuals. Listed below is a broad overview of recognized clinical signs and symptoms. A more thorough review of the published literature is strongly recommended (see Background Reading).

Medical History: Possible source of exposure, identification of risk group exposure, blood transfusion, acupuncture, tattoos, needle stick exposure, foreign travel, and sexual history.

Dermatologic: Kaposi's sarcoma (purple or reddish nodules), which may appear anywhere in the skin and on mucocutaneous surfaces (e.g., mouth and rectum), infectious processes (e.g., Herpes simplex or zoster), seborrheic dermatitis, unexplained diffuse hyperpigmentation, alopecia.

Ophthalmologic: Ocular lesions (retinitis due to cytomegalovirus or toxoplasmosis), cottonwool spots, retinal hemorrhages.

Hematopoietic: Fluctuating adenopathy associated with aching discomfort. Variable lymph node size and consistency. Soft, moderately enlarged spleen. Large, firm spleen and/or very large lymph nodes are suggestive of intracellular infections (e.g., mycobacterium avium), lymphoma or Kaposi's sarcoma.

Gastrointestinal: Oral thrush, candida esophagitis associated with xerostomia and pharyngitis or odynophagia. Watery diarrhea due to various protozoan infestations and lower GI pain due to herpes proctitis.

Pulmonary: Non-productive cough and dyspnea (associated with *Pneumocystis carinii* or viral pneumonitis), productive cough linked to bacterial or other etiology.

Musculoskeletal: Diffuse arthralgias and myalgias associated with febrile prodrome suggestive of vasculitis, autoimmune and rheumatologic diseases.

Neurologic: Persistent headache, memory loss, ataxia, confusion, irrational behavior, personality change, focal neurologic signs, and seizure.

General: Fatigue, asthenia, night sweats or sweating, decreased libido, withdrawal and other signs of depression, fever including Pel-Ebstein fever pattern.

Laboratory tests that could be helpful in evaluating antibody positives include a complete blood count, differential and platelet count, VDRL, tests of hepatitis B infection, and baseline routine chemistries, including gamma globulin levels. Additional, specific tests should be directed by the clinical findings.

Therapeutic Intervention

Therapeutic interventions that are specific for the virus or for the immunodeficiency do not yet exist, although there is considerable research being done attempting to develop such modalities. However, rapid diagnostic evaluation and intervention with appropriate antimicrobials in specifically documented illnesses may be lifesaving. Some clinicians have advocated use of prophylactic therapy to prevent common protozoan and fungal diseases (i.e., trimethoprim-sulfamethoxazole and ketoconazole), but there is also a substantial amount of drug-related dermatologic and hematologic toxicity for some of these agents and implementation of such therapy without consulting a specialist would not be recommended.

What to Tell the Seropositive Patient

From a clinical perspective, counseling a seropositive, clinically healthy individual presents a challenge since the risk of clinical disease is not well characterized. The possibility that the test reactivity represents a biologic false positive should be discussed particularly in the patients without definable risk exposure. It is inevitable that substantial psychological stress will derive from the knowledge of antibody positivity, and judicious reassurance is supported by the current data which suggests that the vast majority of antibody positives are clinically well. However, given the fact that clinical problems may take some years to become manifest clinically, *long-term follow-up with careful assessment of symptomatology* as described above are in order. HTLV-III has also been linked to hematologic and neurologic disorders, a focus of active investigation. With this in mind, clinical symptoms in antibody-positive persons should be pursued vigorously to assure optimal care. The risk for an antibody-positive individual being infectious for another person is not quantified. As summarized above, certain factors (e.g., sexual contact, needle sharing, pregnancy) are linked to virus transmission and may serve as the basis for tailoring recommendations to the antibody positive individual to decrease the likelihood of transmission of the virus.

Summary

The practicing physician encountering an HTLV-III antibody-positive person must deal with incomplete knowledge about the natural history of the disease. Preventive measures and practical advice to the individual are summarized in attached documents. Clinical long-term follow-up of antibody-positive persons should be a commitment for physicians confronted with such patients. Careful monitoring of the fast-moving medical literature concerning this condition is important to provide optimal care. Where feasible, consideration of referral to a center organized to follow such patients may be appropriate.

Background Reading

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Information for Individuals About AIDS and the Antibody Blood Test

[For use in educating donors BEFORE collecting blood or plasma]

Information About the Test for Antibodies to the HTLV-III Virus

WHAT IS AIDS?

Acquired immunodeficiency syndrome (AIDS) is a serious disease which reduces the body's ability to fight infection. Over the past several years increasing numbers of persons in certain high-risk groups developed the disease, and by early 1985 about 9,000 cases had been reported. During 1984, a virus (HTLV-III) was discovered which is the cause of AIDS, and a test was developed to detect antibodies to the virus. More detailed information about AIDS is available in *Facts About AIDS*, which is provided by the U.S. Public Health Service.

WHAT IS THE ANTIBODY TEST?

When a person is infected by a virus, the body's white blood cells normally begin to fight the infection by producing substances called antibodies. Antibodies can therefore be used to indicate whether or not a person has been infected by a virus. Research has shown that antibodies to the HTLV-III virus are usually found in the blood of persons who have AIDS or AIDS-related conditions, and in many people who are members of groups at increased risk for AIDS. However, a negative antibody test does not guarantee that a person is free of the virus, especially if he or she is a member of a group at increased risk for AIDS. Antibodies may not have developed if exposure to the virus was recent. That is why it is very important for members of groups at increased risk for AIDS to continue to refrain from donating blood or plasma. It is also possible that other factors, including other viruses, could cause the test to be positive even though the person was never infected with HTLV-III.

WHAT IS THE ANTIBODY TEST BEING USED FOR?

Until recently, the antibody test was limited to use in research to gain a better understanding of AIDS as an infectious disease. For example, some of those studies showed that 68% to 100% of patients with AIDS had been exposed to the HTLV-III virus. During the past year, commercially available tests for HTLV-III antibody were being developed, and such tests were recently approved by the Food and Drug Administration.* The primary purpose of these antibody tests is to screen blood which is donated for use in transfusion and in the production of other blood products.

WHY IS THE ANTIBODY TEST BEING USED TO SCREEN BLOOD?

Because a positive antibody test means that a person may have been infected by the HTLV-III virus, it is now possible to use the test to identify blood which should not be used for transfusion. By not using blood from people who may have been infected by HTLV-III, we believe that transfusions will be even safer than they are now.

WHAT DOES A POSITIVE ANTIBODY TEST MEAN?

The most important thing to understand is that the antibody test is *NOT a test for AIDS*, and that a positive test does *NOT* mean that the person definitely will develop AIDS. The test does provide an extra safety check on blood so that the risk of getting AIDS from transfusions will be even lower than it already is. As with many other blood tests, there will be some people who have test results which are called "false-positives"; that is, for some reason the test indicates that HTLV-III antibody is present when, in fact, it is not really HTLV-III antibody which is causing the test to register positive. For this reason it is especially important for persons with positive antibody tests to have follow-up tests to try to determine whether or not the screening test really means that HTLV-III antibody is present.

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*This information sheet was prepared on 2/14/85 (before any test was licensed), and it is intended to be used *after* tests are commercially available.

Based on what is known so far, probably only a small proportion of people infected with the virus will develop AIDS. In fact, many infected people may not develop any illness at all. But there is no information at the present time to be able to predict which persons with the antibodies are more likely or less likely to develop AIDS-related conditions or AIDS itself. For that reason, follow-up medical evaluations are strongly recommended.

WHAT WILL BE DONE WITH THE TEST RESULTS?
If the test for HTLV-III antibody is positive when repeated, and we are satisfied that there has not been a laboratory error, we will inform you (insert method to be used, e.g., by letter) and advise you regarding a follow-up medical evaluation. Donors with positive HTLV-III antibody tests will be placed on a list of persons who may not give blood, and the reason for being deferred as a donor will be kept in a confidential file. Only authorized individuals will have access to this information. In the future we may have to report HTLV-III positive test results to the Health Department as is now required for some other tests.

A Special Note to Persons Who May Be At Increased Risk for Aids

It is vital to the safety of the blood supply that persons who are in groups at increased risk for AIDS continue to follow the U.S. Public Health Service recommendations and to voluntarily refrain from donating. These groups are: 1) anyone who has AIDS or one of its signs and symptoms; 2) males who have had sex with more than one male since 1979, and males whose sexual partner has had sex with more than one male since 1979; 3) past or present abusers of intravenous drugs; 4) Haitians who entered the USA after 1977; 5) hemophiliacs; and 6) sexual partners of persons in these groups.

Even though we are now testing blood for antibodies to the HTLV-III virus, the test will not detect all people who may be carriers of the virus because not everyone who is infected with the virus will have antibodies. If you think you are at increased risk for AIDS, or that you may have been exposed to the virus, *DO NOT DONATE BLOOD* even if you feel perfectly healthy. There is a possibility that antibody for the virus may not be detected when your blood is tested even though you may have been infected. If that were to happen, the blood would be used to treat patients who would then be at risk for infection by HTLV-III and for AIDS.

If you are interested in knowing whether or not you have antibody to HTLV-III, see your physician or [insert name and location of other testing site].

Information for Persons Who Have a Positive Test for HTLV-III Antibody

[To be used in conjunction with the pre-donation information which should be offered again with the test results]

A positive HTLV-III antibody test does not always mean that a person has been infected by the virus which causes acquired immunodeficiency syndrome (AIDS). Positive tests in blood and plasma donors may be caused by other things, and that is why a follow-up medical evaluation is important in order to get a better understanding of the meaning of your test results. Your doctor is in the best position to decide what additional tests, if any, need to be done. It is important that you have as open and frank a discussion as possible regarding any possible exposures that you may have had to the virus, so that your physician can make the best evaluation.

Until your doctor has made a medical evaluation, it is best to be cautious, even though you have no symptoms, and to assume that you may have been exposed to the virus, that you may be contagious, and that you might unknowingly spread the virus to others. You will want to take responsible steps to prevent the possibility of spreading the virus to other people, especially your family and close contacts.

— Do not donate blood or plasma, sperm, body organs, or other tissues.

— You should let your doctor and dentist know that you have a positive HTLV-III antibody test so that they can do their best in caring for you and in preventing spread of the virus.

— Limit your sexual contacts, and be frank with your sexual partner(s) about steps you are taking to prevent the spread of the virus. Using a condom may help in this regard.

— Sexual practices in which exchange of body fluids such as semen takes place should be avoided.

- Virus has been found in saliva of some infected people, and it is possible that it could be transmitted by open-mouthed, or "French," kissing and by oral sex.

- There is no evidence that the virus can be spread through casual kissing or other casual social contacts such as hugging. Such contacts with other people at work or in the community do not need to be modified.

- Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.

- If you are a drug user:

  - limit your drug use
  - do not let others use needles you have used and do not use someone else's needles
  - do not leave your "works" around where others might pick up needles

- If you are a woman with a positive antibody test or the sexual partner of a man with a positive antibody test, it would be advisable to avoid pregnancy or to postpone pregnancy until more is learned. Some infants have developed AIDS from their infected mothers.

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Message from Secretary Heckler

Over the past two years, scientists at the National Institutes of Health and others in France have identified the virus that causes AIDS and have developed an antibody-screening test for donated blood. Surveillance by the Centers for Disease Control continues to assess the extent of this growing public health problem and enables the Public Health Service to issue recommendations to health professionals to prevent the spread of this deadly disease. In addition, FDA is encouraging research on drugs and biologics to fight both the virus and the opportunistic infections associated with AIDS.

We have accomplished much in a short time. Yet AIDS continues to spread and the urgency of our educating both health professionals and the general public about this disease increases, as does the necessity of funding research to develop medical treatments and a vaccine for AIDS. I pledge that this effort will continue to be HHS's number one priority.

Sincerely yours,

Margaret M. Heckler

Margaret M. Heckler
Secretary of Health and Human Services

Letter from Commissioner Young

Dear Colleague:

I join Secretary Heckler in recognizing the urgency of finding ways to contain the spread of AIDS and to make available treatments for those stricken.

As with the speedy licensing of test kits for screening blood for antibodies to HTLV-III, FDA is giving highest priority to AIDS-related drugs and biologics. We are providing research incentives through our Orphan Products Development Program and are working closely with manufacturers submitting plans for clinical studies. We also make certain drugs available for "compassionate" or "treatment" use while they are under study.

This special issue of the *FDA Drug Bulletin* summarizes current knowledge about HTLV-III and efforts to prevent its spreading. It augments my previous "Dear Doctor" letter of March 8, 1985. Our publications will continue to keep health professionals informed of progress on AIDS.

Sincerely yours,

Frank E. Young

Frank E. Young, M.D., Ph.D.
Commissioner of Food and Drugs

Progress On AIDS

The identification of the virus responsible for acquired immunodeficiency syndrome (AIDS) has made possible an effective blood antibody screening test and the updating of the AIDS case definition. This causative virus has been named human T-lymphotropic virus type III (HTLV-III) by researchers at the National Institutes of Health (NIH) and lymphadenopathy-associated virus (LAV) by French researchers at the Pasteur Institute.

An intensive research effort is under way to find drugs and therapeutic biologics and a vaccine that could be used to treat or prevent the development of this generally fatal disease.

Blood Supply Safer

Use of screening tests for HTLV-III antibody on donated blood and plasma is successfully preventing the virus responsible for AIDS from entering the blood supply.

Conferees at a July 31, 1985, workshop Bethesda, Md., cosponsored by the National Institutes of Health (NIH), FDA and the Centers for Disease Control (CDC), heard that blood and plasma collecting facilities have begun routine testing for this antibody and that all blood found to be reactive must be discarded. At the workshop, representatives from the American National Red Cross, the American Association of Blood Banks, the Council of Community Blood Centers, the Greater New York Blood Program and the American Blood Resources Association agreed that the tests are effective in protecting the public from receiving blood containing HTLV-III.

FDA reported data from a survey of more than 1.1 million units of blood collected and tested for HTLV-III antibody by 155 centers of the major blood organizations through June 16, 1985.[1] Of this total, 2831 units (0.25%), or about 1 in 400, were reported to be repeatedly reactive for antibody using the licensed enzyme-linked immunosorbent assays (ELISA or EIA) originally developed by NIH scientists.

The pattern of positive tests varied slightly in different regions of the country and according to the manufacturer's test kit used. This frequency of repeatedly reactive donors was consistent with the data obtained in clinical trials conducted prior to the licensure of the three manufacturers' reagents.

CDC and the Atlanta Region of the American Red Cross reported data from testing more than 51,000 blood donors of whom 0.23% were repeatedly reactive.[2] Of 106 repeatedly reactive units, 34 (32%) were strongly reactive and these correlated highly with both positive Western blot tests (94%) and positive culture for HTLV-III (56%). By contrast, in 220 donors whose tests were initially reactive but subsequently negative, as well as in a random sample of 50 donors with completely negative tests, none had a positive Western blot and none had a positive virus culture.

While donors with repeatedly reactive tests are equally distributed between males and females, those with strongly reactive tests that correlated closely with positive Western blot and virus culture results were more apt to be male.

Of repeatedly reactive donors interviewed, 89% of those with strongly reactive tests were found to have identifiable risk factors for HTLV-III infection, while none of those with weakly reactive tests had risk factors. Thus, of the approximately 3 in 1200 blood donors found to be repeatedly reactive, about 1 in 1200 will likely be infected with HTLV-III, while about 2 in 1200 will probably be representative of nonspecificity in the test rather than infection.

The reason for this nonspecificity is unknown but probably represents, at least in part, the effect of antibody directed against the human cells used to grow the virus in producing test reagents.

To measure test sensitivity, antibody tests and virus isolation attempts were made on blood samples from high-risk persons attending a clinic for sexually transmitted diseases in San Francisco. None of 70 men with negative HTLV-III antibody tests had a positive virus culture; 43 (60%) of 72 with repeatedly reactive tests were culture-positive. Among these 72 antibody-positive blood samples, 70 (97%) were highly reactive and 97% of those tested to date had a positive Western blot test as well.

Plasmapheresis facilities are generally notifying donors when a repeatedly reactive EIA test result is obtained. Blood banks at present are often seeking confirmation of EIA reactive results by Western blot before notifying donors.

Fewer than 2% of reported AIDS cases have been thought to be transmitted by blood transfusion. Even this risk will be virtually eliminated with the application of the new test coupled with the continued use of self-exclusion criteria for high risk donors.

In September 1985, these criteria were broadened to include not only members of high-risk groups,[3] but also any man who has had sex with another man since 1977, including those who had only a single homosexual experience. This change was prompted by the discovery that the majority of individuals having confirmed positive HTLV-III test results have been homosexual or bisexual males who felt they were not in a risk group.[4]

Because the incubation period for AIDS can be more than five years, new cases of transfusion-associated AIDS can be expected to appear for some time in persons infected with HTLV-III before the blood screening test came into use.

In addition to its use in screening donated blood, Public Health Service (PHS) has recommended that the EIA for HTLV-III antibody be used to screen blood and serum from donors of organs, tissue or semen intended for human use, and that the test result be used to evaluate the appropriate use of such materials from these donors.[5]

Data have established that hemophilia A patients treated with Factor VIII concentrates had a significantly greater risk of contracting AIDS than any other blood (or blood product) recipient group.[6] Recent adoption of heat (or chemical) processes to inactivate viruses, including HTLV-III, by U.S. licensed manufacturers of Factor VIII, together with the screening of the blood supply, have now virtually eliminated this risk. Factor IX concentrate, used to treat hemophilia B, has only rarely been thought to transmit HTLV-III; however, a viral inactivation step is being added to its manufacturing process as well.

FDA Letter

In a letter mailed to physicians in March 1985, preceding the approval of the first EIA test kit, FDA emphasized that the screening kits do not constitute a diagnostic test for AIDS, but rather are useful to identify—through the presence of antibody—those who have been infected by HTLV-III and therefore might transmit the disease. As with any serologic test, there will be some false-positive results even in repeatedly reactive samples. These apparently aberrant results may represent biologically false-positive reactions such as cross reactivity to other antigens or nonspecific reactions. Positive antibody test results are more likely to be a true indication of HTLV-III infection when the prevalence of infection by the virus in the population being screened is higher.

PHS Recommendations

PHS has issued recommendations for screening donated blood for HTLV-III antibody.[7] Summarized, these include:

- Screening all plasma and blood for HTLV-III antibodies.
- Blood or plasma that is reactive for HTLV-III antibody should not be transfused or used for manufacture into injectable products capable of transmitting infectious agents.
- Notifying the donor only upon a positive result from a second EIA or other test (e.g., Western blot) and referring the donor to a physician for evaluation.
- Keeping positive test results confidential. Whenever possible, donor deferral lists should be general, without specifying the reason for inclusion on the list.

Recommendations For Patients With Reactive Tests

Physicians and other health practitioners whom patients consult after having been told they have repeatedly reactive test results can advise their patients of the following: [7]

- The prognosis for an individual infected with HTLV-III over the long term is not known. However, data suggest that most persons will remain infected for life.

- Even though asymptomatic, persons with repeatedly reactive HTLV-III antibody tests may transmit infection to others through sexual intercourse, sharing of needles and, possibly, exposure of others to saliva through oral-genital contact or intimate kissing. Recent research has revealed that HTLV-III is also present in the tears of AIDS patients but there is no evidence of transmission through tears. The efficacy of condoms in preventing infection with HTLV-III is unproven, but the consistent use of them may reduce transmission. Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.
- Regular medical evaluation and follow up is advised, especially for patients who develop signs and symptoms suggestive of AIDS.
- Persons with repeatedly reactive HTLV-III antibody tests should not donate blood, plasma, body organs, other tissue or sperm.
- Women with repeatedly reactive antibody tests or whose partners are seropositive, are at increased risk of acquiring AIDS. If they become pregnant their offspring are also at increased risk.
- If persons with repeatedly reactive antibody tests have accidents involving bleeding, contaminated surfaces should be cleaned with household bleach freshly diluted 1:10 in water.
- When seeking medical, dental or eye care, these persons should advise the practitioner of their positive antibody status so that appropriate evaluation can be undertaken and precautions can be taken to prevent transmission to others.
- Devices used on these patients that have punctured the skin (such as hypodermic and acupuncture needles) should be steam-sterilized by autoclave before reuse or safely discarded. Whenever possible, disposable needles and equipment should be used.
- Testing for HTLV-III antibody should be offered to persons who may have had intimate contact with seropositive individuals (e.g., sexual partners, persons with whom needles have been shared, infants born to seropositive mothers).

Patients and their families can also be advised there is no evidence that HTLV-III is transmissible by casual contact including: living in the same house as an infected person; caring for an AIDS patient; eating food handled by an infected person; being coughed or sneezed upon by an infected person; casual kissing; or swimming in a pool with an infected person.

As with most other infectious diseases, the spectrum of responses to HTLV-III infection is varied. Because it represents the end of the spectrum, AIDS is the most easily recognized of these responses. But as with other viruses (e.g., poliomyelitis), infection with HTLV-III probably does not inevitably result in the worst outcome. Preliminary estimates by CDC suggest that fewer than approximately 10% of those infected have thus far developed AIDS; approximately 25% have had only relatively minor problems such as chronic lymphadenopathy. About two-thirds of infected persons have remained asymptomatic, at least in the short term.

Precautions For Health Care Practitioners

PHS previously recommended procedures for lab personnel,[8] dentists and morticians[9] having contact with AIDS patients.

Recently, after NIH scientists isolated HTLV-III virus in tears, NIH, CDC and FDA issued recommendations in the *Morbidity and Mortality Weekly Report* of Aug. 30, 1985 (34:533-534). Summarized, they are:

- Health care professionals performing eye examinations or other procedures involving contact with tears should wash their hands immediately after a procedure and between patients. When practical and convenient, disposable gloves should be worn. The use of gloves is advisable when there are cuts, scratches or dermatologic lesions on the practitioner's hands.
- Instruments that come into direct contact with external eye surfaces should be wiped clean and then disinfected by:

a) a 5- to 10-minute exposure to a fresh solution of 3% hydrogen peroxide, or

b) a fresh solution containing 5,000 parts per million (mg/L) free available chlorine—a 1/10 dilution of common household bleach (sodium hypochlorite), or

c) 70% ethanol, or

d) 70% isopropanol.

The device should be thoroughly rinsed in tap water and dried before reuse.

- Contact lenses used in trial fittings should be disinfected between each fitting. Hard lenses, rigid gas permeable lenses, and soft lenses should be disinfected with a commercially available hydrogen peroxide contact lens disinfection system currently approved for soft contact lenses. Alternatively, some hard lenses and soft lenses can be disinfected by heat disinfection. Rigid gas permeable lenses may warp if heat-disinfected.

Case Definition

As originally defined,[10] the clinical definition of AIDS follows four major patterns:

(1) A febrile prodrome of weeks to months followed by opportunistic infection

(2) Abrupt onset of opportunistic infection

(3) Presentation with Kaposi's sarcoma

(4) Progression from AIDS-related complex.

As a result of the identification of HTLV-III and the development of reliable blood screening tests, this case definition was revised by CDC in June 1985 in response to recommendations by the Conference of State and Territorial Epidemiologists (CSTE)[11] and now includes the following refinements:

- In the absence of the opportunistic diseases required by the current case definition, any of the following diseases is considered indicative of AIDS if the patient has a positive serologic or virologic test for HTLV-III:
  - —disseminated histoplasmosis (not confined to lungs or lymph nodes) diagnosed by culture, histology or antigen detection
  - —isosporiasis, causing chronic diarrhea (more than 1 month), diagnosed by histology or stool microscopy
  - —bronchial or pulmonary candidiasis, diagnosed by microscopy or by presence of characteristic white plaques grossly on the bronchial mucosa (not by culture alone)
  - —non-Hodgkin's lymphoma of high-grade pathologic type (diffuse, undifferentiated) and of B-cell or unknown immunologic phenotype, diagnosed by biopsy
  - —histologically confirmed Kaposi's sarcoma in patients who are 60 years old or older when diagnosed.
- In the absence of the opportunistic diseases required by the current case definition, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis in a child (under 13 years of age) is considered indicative of AIDS unless test(s) for HTLV-III are negative.
- Patients who have a lymphoreticular malignancy diagnosed more than 3 months after the diagnosis of an opportunistic disease used as a marker for AIDS will now be included as AIDS cases.
- To increase the specificity of the case definition, patients are excluded as AIDS cases if they have a negative result on testing for serum antibody to HTLV-III, have no other type of HTLV-III test with a positive result, and do not have a low number of T-helper lymphocytes or a low ratio of T-helper to T-suppressor lymphocytes. In the absence of test results, patients satisfying all other criteria in the definition continue to be included.

In accordance with these recommendations, only AIDS—the more severe manifestation of HTLV-III infection—will be reportable nationally. The reportability of milder disease associated with HTLV-III infection (AIDS-related complex [ARC] and persistent generalized lymphadenopathy [PGL]), as well as asymptomatic infections will continue to be determined by individual states.

ARC is a clinical and laboratory syndrome characterized by minor conditions clinically associated with immunosuppression (e.g., oral thrush) and laboratory evidence of immunosuppression probably associated with HTLV-III infection. In addition, unexplained idiopathic thrombocytopenia is probably associated with HTLV-III infection, as are a variety of non-life-threatening fungal, viral and bacterial infectious processes that probably represent manifestations of virus-induced immunologic perturbation. These manifestations are sometimes termed lesser AIDS.

PGL is also recognized as being associated with HTLV-III infection. It is a symptom complex characterized by the occurrence of persistent, unexplained lymph node enlargement in several extra-inguinal lymph node groups. The relationship of the lymphadenopathy syndrome to progression to overt clinical AIDS is uncertain but probably is as high as 10%. (Of course, physicians are aware that PGL can be caused by agents other than HTLV-III.)

Approaches to clinical evaluation of AIDS and its diverse related clinical disorders were discussed in PHS informational material mailed by FDA to physicians on March 8, 1985. Health professionals who did not receive this information may obtain it from: FDA (HFI-40), 5600 Fishers Lane, Rockville, MD 20857.

Epidemiology

CDC reports the following epidemiological description of AIDS cases:

Between June 1981 and Sept. 16, 1985, 13,228 persons in the United States were reported to have been diagnosed as having AIDS. Of these, 6758 (including 116 children) are known to have died. Of the total number of cases, 57% had *Pneumocystis carinii* pneumonia (PCP) without Kaposi's sarcoma (KS); 19% had KS without PCP; 18% had opportunistic infections without KS or PCP; and 6% had both KS and PCP. Seventy-three percent of the adult/adolescent cases occurred in homosexual or bisexual males; 17% in intravenous drug abusers; 1% (92 cases) in patients with hemophilia or other coagulation disorders; 1% (133 cases) through heterosexual contact with a person who had AIDS or who was at high risk (of these, 118 cases occurred in women and 15 in men); 2% (204 cases) through transfusion with blood or blood products; 6% (829) in none of these categories.

Seventy-one percent of the pediatric cases occurred in children whose parents had AIDS or were at increased risk for AIDS, with epidemiologic data suggesting transmission from infected mother to child before, at, or shortly after birth. Five percent occurred in children with hemophilia or other coagulation disorders; 16% in those who had received blood or blood products transfusion; and 8% in none of these categories.

The highest number and percentage of AIDS cases were reported in New York State (35%, 4669 cases). California followed with 23% (3067 cases). Florida reported 7% of the cases, New Jersey 6%, and Texas 5%. The following each reported 2% of the cases: Pennsylvania, Illinois, Massachusetts, Georgia and the District of Columbia. The following each reported 1% percent of the cases: Maryland, Puerto Rico, Washington, Connecticut, Louisiana, Virginia, Colorado, Ohio and Michigan. The following each reported 10 or more cases but less than 1% of the cases: North Carolina, Missouri, Arizona, Indiana, Iowa, Hawaii, Kansas, Oregon, Minnesota, Wisconsin, South Carolina, Alabama, Kentucky, Tennessee, Oklahoma, Rhode Island, Utah, Delaware, Nevada, Iowa, New Mexico, West Virginia and other states and territories. The only states reporting no cases were Montana, North Dakota and South Dakota.

The number of cases per million population is 58.1 for the entire United States but varies greatly in different metropolitan areas. In New York City, from June 1981 to Sept. 16, 1985, there were 471.9 cases per million population, and in San Francisco there were 461.8 cases per million population. The three other metropolitan areas with the highest cases per million were Miami, Fla., with 270, Newark, N.J., with 166.3, and Los Angeles with 150.5. In contrast, areas outside these metropolitan areas had 27.1 cases per million population.

Prevention and Treatment

Many agents have been used to combat the multitude of infections to which AIDS victims are susceptible. Although some of these treatments have been effective in temporarily halting these infections, the persistence of the underlying immune defect ensures that they will recur or be replaced by other equally serious infections.

The only hopes for curing AIDS are by attacking and destroying the HTLV-III virus or correcting the underlying immune defect. Because there is no specific therapy for AIDS at the present time, it is necessary to take certain prevention and education measures to reduce the threat of AIDS and create a better awareness of the disease. This has generally been accomplished as new information develops through communications from various PHS agencies.

As with many other viral diseases, the most effective way of preventing AIDS is through the use of a vaccine that would protect against HTLV-III infection. NIH scientists have initiated a major effort to develop a vaccine. This involves searching for antigenic components of the virus that would be capable of stimulating the production of virus-neutralizing antibodies. A number of novel approaches are being explored including several that involve application of the new recombinant DNA technology. Several of these experimental preparations have been inoculated into animals and any that appear promising will be scheduled for clinical trial in small numbers of volunteers.

A major effort is under way to find drugs that would be effective in treating AIDS patients and others already infected with the virus. The status of such research was discussed at a workshop cosponsored by NIH, FDA and CDC, held at NIH on June 3, 1985. Participants from around the world discussed studies conducted with antiviral agents that suppress the replication of HTLV-III and with other substances capable of stimulating the damaged immune system. Now that methods for propagating HTLV-III in the test tube are widely available, *in vitro* screening of drugs for antiviral activity can be quickly accomplished. Thus, many compounds in addition to those already under study will be identified as deserving of clinical evaluation.

Although to date no treatment has been proven to effectively combat HTLV-III infection, several agents are already under investigation. Those discussed at the workshop, at other professional meetings, in the literature and in the news media fall into two categories—antivirals and immune stimulators.

ANTIVIRALS

HTLV-III has an envelope that is heavily glycosylated. A retrovirus, HTLV-III uses its RNA to produce a DNA which in turn produces the RNA responsible for the viral proteins. The production of the DNA is dependent upon the viral enzyme, reverse transcriptase (RT). Theoretically, an effective agent would either effect a change in the viral envelope, alter the membrane of the target cell to prevent adsorption of the virus, or interfere with one of the steps in the viral replication, such as RT. The latter has been the presumed mechanism of action of most antiviral agents investigated to date. Because RT-inhibitors can potentially damage normal cells at high concentrations, research is focused on the development of RT-inhibitors that have an acceptable margin of safety.

Suramin and ribavirin are two of the antivirals currently in clinical trials in the United States. There is evidence that suramin has activity against HTLV-III virus both *in vitro* and *in vivo* [12,13] but no clinical benefit has been shown thus far. In a 6-week study of eight patients at NIH, HTLV-III was cleared from the blood of four patients, but no clinical improvement was noted in any of the patients and the virus returned when the medication was stopped. Similar results were reported in a study of three patients at Walter Reed Medical Center and in a study of 16 patients in France. All patients in the U.S. studies and many of those in the French study developed toxic reactions including rash, proteinuria and pyuria, elevated liver transaminases and hepatitis, and burning sensations of the extremities. This drug has been used on an investigational basis for many years to treat trypanosomiasis and onchocerciasis.

Ribavirin has shown some activity against HTLV-III *in vitro*.[14] In one trial in New York, 27 asymptomatic gay men with HTLV-III infection received an oral formulation of ribavirin in varying dosages. RT activity in cultures of peripheral blood lymphocytes decreased but was not eliminated during treatment. Dose-related side effects included: anemia, nausea, flatulence, headache, fatigue, dry mouth, mental status changes, and dyspnea on exertion. Other studies are ongoing.

Alpha-interferon, a leukocyte-derived protein with antiviral, immunomodulatory and anti-cancer properties, has been shown to inhibit HTLV-III replication *in vitro*. When given to patients with AIDS and Kaposi's sarcoma, about half of the patients had some evidence of reduction in tumor burden, although in many patients the response was transient. More data are needed to determine whether the agent contributes to improved overall survival. Studies are ongoing at Massachusetts General Hospital.[15,16]

In studies abroad, two other antivirals, phosphonoformate (also called PFA or Foscarnet) and HPA-23, have shown some activity against the AIDS virus *in vitro*. PFA is also known to have activity against several herpesviruses, which commonly cause severe and protracted secondary infections in patients with AIDS. Clinical trials of PFA in viremic patients with ARC or AIDS are under way in Denmark and Sweden. The major known side effect of PFA is nephrotoxicity.[13] It is also retained in bone tissue for long periods.

In French studies, HPA-23 has been shown to reduce or clear virus transiently from the blood in some cases. However, no clinical improvement was noted in the 19 patients (7 ARC and 12 AIDS) studied. Viremia reappeared after discontinuation of therapy. Thrombocytopenia, bleeding and hepatic dysfunction are common side effects of this drug[15,16] and are dose-limiting. FDA has approved limited clinical trials of HPA-23 in patients with AIDS. Those trials will begin this fall in five U.S. medical centers.

Another substance, compound BW A509U, a thymidine analogue, has shown *in vitro* activity against HTLV-III. Clinical trials with BW A509U have also been approved and are in progress at Duke University and NIH.

Both HPA-23 and BW A509U have been designated orphan drugs for the treatment of AIDS after application for this status was made by Rhone-Poulenc Pharmaceuticals in the case of the former, and Burroughs Wellcome Co. in the case of the latter. An orphan designation is a way of facilitating early testing of drugs and biologics for rare diseases, including AIDS, by providing tax credits, grants and exclusive approval protection as authorized by the Orphan Drug Act

Another antiviral agent being considered for investigational use in U.S. patients with HTLV-III is ansamycin, a drug used experimentally in this country to treat *Mycobacterium avium intracellulare* infections, a common opportunistic infection in AIDS patients. (See December 1982 *Drug Bulletin*.) Ansamycin has been shown to have *in vitro* activity against HTLV-III/LAV. In addition, widespread screening of chemicals for activity against HTLV-III/LAV has identified several other compounds which are being readied for clinical trials.

In evaluating these agents, FDA is considering separately their potential effectiveness in asymptomatic carriers of HTLV-III, in ARC and PGL, and in frank AIDS, as it is possible that some agents useful in one may not be useful—and could even be detrimental—in the others.

IMMUNE STIMULATORS

A central component of the immune system, the T-4 lymphocyte, is infected and destroyed by HTLV-III. Because many of the functions of the helper/inducer (T-4) lymphocyte are carried out through soluble protein messengers normally produced by the human body, such as interleukin-2 (IL-2) and gamma interferon, these substances are among those being investigated in the treatment of patients with AIDS.

Based upon the observations of PHS scientists in early 1982 that IL-2 was capable of enhancing the killer cell activity of lymphocytes from AIDS patients, initial clinical trials of this compound began in June 1982.[17] Preliminary results indicate that IL-2 can enhance the lymphocyte count and cause a minor reduction in size of KS tumors in some patients. But neither of these effects by itself has caused significant clinical improvement in the overall clinical status of AIDS patients.[15]

Trials of gamma interferon at NIH from February 1983 to September 1984, in a wide range of doses, showed no clinical benefits to the 25 patients involved. Therefore, trials to study the immunorestorative properties of gamma interferon in patients with AIDS were discontinued. However, the National Institute of Allergy and Infectious Diseases (NIAID) is currently sponsoring a trial of this compound in the treatment of *Mycobacterium avium intracellulare* infections in AIDS patients at Cornell University.[15]

Other immune modulators under investigation for treating AIDS include isoprinosine and thymopectin. Partially through funding provided by an NIAID cooperative agreement, isoprinosine was studied at St. Luke's-Roosevelt Hospital in New York. The study included a small number of patients with AIDS and related illnesses. This study failed to reveal any clinical efficacy of the drug and showed minimal effects on immune parameters measured *in vitro* from patients with AIDS-related illnesses.[15] Thymopectin, a thymic hormone, is being studied at the University of California at Los Angeles (UCLA) under a cooperative agreement with NIAID.[16]

Immunoglobulin therapy is being investigated in the treatment of AIDS in children. It is a unique feature of pediatric AIDS that the patients' immune systems are destroyed before they have had a chance to develop fully.[15]

Some scientists have speculated that it may prove necessary to use a combination of therapies to treat AIDS. Combination therapy involving immunotherapy and antiviral drugs is under way in a study of three patients with AIDS, all of whom have healthy identical twin brothers. The three AIDS patients are being treated at NIH with a combination of suramin and bone marrow transplantation. A study combining suramin and IL-2 in other patients is being planned.

Treatment of Opportunistic Infections and Malignancies

A number of drugs are under investigation for treating the malignancies and opportunistic infections associated with AIDS. Marketed drugs used to treat PCP include trimethoprim/ sulfamethoxazole and pentamidine isethionate. The latter was approved for use in patients with PCP after receiving support from FDA's Office of Orphan Products Development. (See December 1984 ***Drug Bulletin***.) Many of the clinical and laboratory studies of this drug were conducted by CDC and FDA. Other agents under investigation for treatment of PCP include dapsone, trimetrexate and alpha-difluoromethyl-ornithine (DFMO).

Other drugs are being investigated for treating AIDS patients with Kaposi's sarcoma, *Mycobacterium avium intracellulare* (see December 1982 *Drug Bulletin*), cytomegalovirus, *Candida albicans* and *Cryptococcus neoformans*. With a disease as serious as AIDS, it is extremely important that there be a concerted effort by the medical community to develop treatments and preventive measures. FDA is encouraging the development of products for use in treating patients with AIDS and other manifestations of HTLV-III infection through a number of mechanisms. FDA works closely with NIH, manufacturers, and academic scientists in the planning of preclinical and clinical studies of drugs and biologic substances for AIDS. With this joint effort, approval for a newly filed investigational new drug application (IND) can be granted in a matter of days and amendments to the original protocol agreed to by telephone as all parties work together to closely monitor the progress of patients under study. FDA scientists in FDA laboratories on the NIH campus collaborate with other groups involved in AIDS research. They are participating in the *in vitro* screening of antiviral drugs and immune stimulators and in the evaluation of patients on experimental treatments at the NIH Clinical Center. This integration of FDA into the total AIDS effort guarantees that, as was the case with the HTLV-III antibody test, any promising product will get rapid regulatory review and become generally available in the shortest possible time.

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SPECIFIC PROJECTS UNDERTAKEN

Dr. YOUNG. Specific projects we will undertake include: the followup and evaluation of blood donors who are found positive by the HTLV–III screening test to determine the medical significance of a result of an individual and the risk associated with blood donations from persons who have developed antibodies to HTLV–III; a study of the impact of additional tests for HTLV–III virus and other retrovirus on the safety of the blood supply—this will be extremely critical; and a study to determine whether HTLV–III is present in feces to investigate transmission in animal models. We will also be involved in additional quality control monitoring of test kits for HTLV–III; review and approval of second and third generation tests for AIDS, and development of adequate methods for collecting and analyzing adverse reactions reports associated with drugs and biologics.

We are extremely pleased to have this opportunity to speak to your committee, a committee I usually do not have the privilege of addressing. I will be delighted to provide information in answer to questions or any other followup information we could provide to do our part with the entire Government and private sector in meeting the needs to overcome this most significant and greatest health priority in the Nation.

Thank you.

Senator WEICKER. Thank you very much, Dr. Young. I appreciate your willingness to appear before the committee. We will be working closely with Senator Cochran.

It is my understanding, Dr. Mason, that the moneys already appropriated, or those contemplated to be sent to the committee, include the clinical trials of four drugs in the sense of those drugs being used to stop the shedding process or the propagation of AIDS. Again, I am not a scientist. I am merely expressing my layman's knowledge. If I am not mistaken, somebody can correct me, there are really two tracks we are talking about here. That is one of vaccine——

Dr. MASON. That is correct.

Senator WEICKER [continuing]. Which is the long-range solution to the problem, and the other track being that of the use of drugs in order to halt this process; am I correct?

Dr. MASON. That is correct. There are two related approaches, one that deals with the discovery, the preparation, the making generally available a vaccine which would allow us to immunize people prior to their coming in contact with the virus. That is proceeding down one track. There is a separate track, with ongoing communication between them looking at chemotherapy. This track will specifically attack the virus after the person has been infected. As Dr. Wyngaarden mentioned, the therapy track bifurcates into two parts because one must lead to something that will destroy the virus in the body. Since these patients may have an immune system which has been destroyed by the virus, you not only have to get rid of the virus but there has to be a way to restore or enhance the immune system, but these drug development activities are proceeding along two major tracks.

Senator WEICKER. I understand. It is my understanding in that area of drug testing that the budget contemplates or there is actually ongoing now or will shortly be ongoing clinical trials for four of these drugs, is that correct?

Dr. MASON. Is that right, Dr. Wyngaarden?

Dr. WYNGAARDEN. Yes; you are talking about the most recent identification of new initiatives. The NCI and NIAID will develop and carry out an elaborate plan for the development and testing of drugs for the treatment of AIDS, as well as opportunistic infections. The plan now is to undertake four such studies within the next year. That depends, of course, upon the rate of development of new opportunities, but in each of those initiatives, there is a great spectrum of work anticipated starting with the testing of chemicals for antiviral activity, as inhibitors of the enzyme specifically found in this virus, the testing, carrying this into phase I, II, and III studies. We have estimated costs for the whole process and the plan is and hope is to be able to do that on four agents.

Senator WEICKER. Then the question is from an operations standpoint—from an appropriations standpoint—are there additional drugs which you or any of your colleagues would like to see clinically tested at this juncture? If so, I gather there is pretty much a rule of thumb as to each one of these trials' costs. Obviously, there would be a financial impact on what it is you would need in appropriations.

Dr. WYNGAARDEN. I think if you would like more specific information on that, Dr. DeVita, in whose Institute these drugs are first tested, might say a few words on that.

Senator WEICKER. Again, let me repeat my question, which I know you understand, Dr. DeVita, is the number four being set by our appropriation or indeed is the number four being set by your scientific evaluation as being the appropriate number right now? Is it being set by me? Is it being set by OMB or being set by you, the scientists, this number four? I obviously have a distinct bias that it should be set by you, not by me or anybody else.

Dr. MASON. In the President's amended budget that includes the $126 million for fiscal year 1986, there was an expansion of effort to develop antivirals which brings NIH up to the level of four, which was their request. In the request for the additional money I mentioned that has not yet come through the system, we have taken into consideration that there well may be additional agents. In fact, NIH has tested over 100. Of course, all of those are not showing promise. We do not want to be in a position where we cannot move ahead with dispatch on any reasonable number. I don't think four is necessarily sacred or holy, it is where we were when that budget was put forth. Now things have changed.

I should also mention, in addition to what is happening at NIH, there is much interest in the private sector. It is important that we do everything we can to enhance and encourage so that this work does not become just a Federal effort. It must be cooperation between the public-private sectors. Dr. Young has outlined things he has been doing to facilitate private sector contributions. The four are those that NIH is planning to work on. We want, however, to enhance that through the private sector and enhance our own ability to move ahead with more drugs.

Senator WEICKER. Thank you very much, Dr. Mason.

Dr. DeVita, would you like to expand?

Dr. DEVITA. Yes, Senator.

Actually the number four was set by us as the number of drugs that we can get into clincial trial very quickly at the present time, although there are more than four candidate drugs. Our plans include starting with four, because we never complete testing in one year on a set of drugs like these. There is a carryover of about two drugs per year, so the number will expand. Two drugs are already in their early stages of testing and ready to go into later stages of testing.

So we need to adjust two more drugs in our expansion. I might add that we do have several very interesting candidate drugs.

Senator WEICKER. I have one more question, one broad question before those asked by Senator D'Amato. I received from a member of the press the following question: How can casual contact be ruled out when the virus has been isolated in tears and saliva? I was going to ask the question. I want to go back to your testimony, Dr. Mason, prepared testimony, where you said:

> We know now that infected mothers can transmit the virus to their babies across the placenta and likely through breast milk. Although the AIDS virus has been isolated from human saliva and tears, there is no evidence transmission has occurred through these routes. There has not been a single case of AIDS reported to us in family members of AIDS patients, except for sexual partners and children born to infected women. In studies of over 300 household contacts, not one person, other than sexual contact or child born to an infected mother, became seropositive or developed AIDS as a result of living with AIDS patients. Studies of more than 1,472 health care workers who have close contact with very ill, often hospitalized, AIDS patients, not one has developed AIDS or become seropositive as a result of contact with patients other than through needle stick injury.

I would like you and anybody else who cares to respond to this very important question, probably the most important question, the transmissibility of AIDS, and I might as well start out with the question given through the Chair, how can casual contact be ruled out since the virus has been isolated in tears and saliva?

Dr. MASON. I won't repeat what you have already read back from my testimony. It was included in the testimony after careful review with all the people here, including Dr. Fauci and Dr. DeVita. I wanted to be sure we all agree 100 percent with the carefully worded statements. I will say again there is no evidence for casual transmission of AIDS from person to person. It is based upon studies that were summarized in my testimony.

Coming back to tears and saliva, if virus is present in high quantity in blood, one would almost assume that you could find virus at some time or another in other body fluids. In other words, when our investigators found virus in saliva and tears, this did not surpise us. We would have been shocked if it could not be found there. We have not found it in feces, in urine, in menstrual blood, or in cervical secretions. I don't believe this is because it isn't there. We just don't have the ability to separate out toxic substances in those fluids that inhibit the growth of the virus in the cultures. In other words, we expect in a blood-borne disease to find virus in other body fluids.

Why then aren't we concerned about transmission? First of all, there is no epidemiological evidence as we have followed contacts of these cases. We have also studied saliva. If we have 50 individuals with virus in their blood, we don't find virus in the saliva of all 50. We find it in approximately 1 out of 50. Then, looking at the quantity of virus in blood versus saliva, we find high quantities in the blood, and very low quantities in saliva. The mere presence of a pathological organism in some fluid does not mean that it represents an effective route of transmission.

We know, for example, with hepatitis-B, which is another blood-borne disease with many similarities to AIDS, you can find it in saliva and yet this is not the way it is transmitted. It is a blood-borne sexually transmitted disease as well. So it isn't surprising that we can isolate AIDS virus in saliva and tears. It is in low quantities and it isn't always there. We need to move away from the belief of the public that one virus equals one infection. Each disease has its own pathogenicity. Comparing AIDS virus with hepatitis-B with regard to clotting factors, factor 8 and factor 9 for example. You can't inactivate a hepatitis-B virus by the heat treatment currently being used to inactivate AIDS virus. The AIDS virus is more susceptible to heat than hepatitis-B virus.

With regard to studies of health care personnel, we are not just looking for symptoms in those 1,400 individuals. Their blood is tested periodically to see whether they have even become positive for the AIDS antibody. That is how carefully they are being studied. They have not been infected by being in close contact with AIDS patients.

With needle stick injuries, we do everything we can in the health care field to prevent someone from sticking themself with a needle after they have drawn blood or administered a medication. In the millions of contacts between health care personnel and sick people, these inadvertent needle sticks occur. With hepatitis, about 26 percent of those who inadvertently pierce themselves with a needle come down with hepatitis-B.

We have been following several hundred people who have stuck themselves with a needle that has been in the bloodstream or inside the tissues of an AIDS victim. In reviewing the medical literature, we find one case described in a British publication. Two other cases also have been identified among several hundred inadvertent needle sticks. We found three while many more would be expected if AIDS were transmitted as easily as hepatitis-B. Yes, AIDS is a fearful disease. We want to be prudent. We want to bend over backward to protect the public health. The public health has to be put at a higher level of importance than the well-being of a single individual. Being prudent though, we can say that AIDS is not a disease that is spread like tuberculosis. If it were the epidemiology would be different. The outcome of these studies would be different. There is good scientific evidence to illustrate why it is not being transmitted by person-to-person contact.

We can't give absolutes. This is what the public would really like. They would like us to say it will never occur and we would like to be able to say that. In science, however, we don't deal with absolutes. With regard to schoolchildren, if parents demanded absolutes for everything, we wouldn't heat the school because the boiler might explode. You can't say absolutely the boiler is not going to explode. Nor can I guarantee when we walk out of our front door tomorrow morning that lightning won't strike us. We can't be that absolute.

We can say, however, that it is very unlikely that such will occur. That is what we are talking about in terms of casual spread of AIDS. It is as unlikely to about the same degree, as school boilers exploding or people being struck by lightning, that someone will get AIDS through casual contact. Sometime with millions of people interactions, something may occur, but the probability or risk is very low. We feel that we are not compromising public health when we say AIDS isn't spread casually.

Senator WEICKER. That is something in which the other members of the panel and those concerned at NIH concur?

Dr. WYNGAARDEN. Yes; we do.

Dr. YOUNG. Yes.

Senator WEICKER. Senator D'Amato?

Senator D'AMATO. Thank you, Mr. Chairman.

First of all, let me commend you for calling this hearing, not only for the purposes of ascertaining what the adequate funding levels can and should be, and whether or not more resources are necessary in the battle against AIDS, the spread of the virus itself, but more importantly, to deal with the fear factor, the tremendous emotionalism, notwithstanding the poll a certain newspaper reported today. I have always had doubts about polls myself, having seen today's nationwide poll, I would say to you it certainly is not—one of my aides—one of my legislative people—[laughter]—just handed me this clip. I know the name of the paper. I know it is on the front page of the paper, and it is printed here in Washington. There is really public concern but not panic, the survey says. That may be true nationwide, but let me say in certain areas of the country, that is not the case.

This is not an accurate reflection of the mood of the people in the New York metropolitan area, and not in other regions where the percentage, vast number of AIDS people have been detected who have the disease. The fact is that it has reached emotionally high levels, and I think understandably so. There has been a lack of information, credible information which the people can deal with. Consequently, we have opportunities where thousands of schoolchildren have been withheld from going to school.

We have litigation. We have questions asked whether or not in New York one of the children—talking about an AIDS victim—is really indeed an AIDS victim. There seems to be doubt as to a young girl being allowed in the school system. Is she an AIDS victim, is the AIDS in remission, et cetera? It is the kind of thing that necessitates our moving forward with an information center. I know you do have a hotline at the present time where people can call—I believe CDC runs it. I think that is good. It seems to me from what I have heard, however, that it is not in service 24 hours a day. Sometimes people have to call another number to be referred to a number, so they can ask questions about transmission, about where to go for help, about how to find out if someone is a carrier. I am going to ask these questions myself, and I would like to know if there are answers to these questions.

Let me ask you this, what would be the cost of funding a full service information center run by the Centers for Disease Control for people to get the relative, necessary, pertinent information so they don't have to deal with little glitches of information that they pick up, whether it be from the media or from person to person. One person may hear something and not really know where they heard it from. Before you know it, what they heard becomes the truth, and the fear factor may then increase manyfold. What would that kind of center cost? Do you believe it is necessary?

Dr. HOPKINS. I can't give you an exact figure today as to what such a center would cost. We can certainly estimate it for the record. I would also say though I think one needs to move beyond a central place where people can call in. One of the things we have been trying to do with our sister agencies in the Public Health Service is to get factual information out. I think one of the other aspects of the concern about the possibility of AIDS transmission through casual contact is not only that people are unnecessarily afraid for themselves and for their children, but also that it takes their eye off the ways in which we know this disease is transmitted. Part of the fear is people think this virus is coming at them from all directions, they can't see it and they can't do anything about it. In fact, as Dr. Mason has said, we do know the way this disease is transmitted in most instances and that people can take specific actions to protect themselves against sexual transmission, and against risks associated with transmission through use of blood products or contaminated needles. To relay this type of information effectively, I think one would need to move conceptually beyond any central place where people could call in.

Senator D'AMATO. Let me ask you this, could you develop those figures for us by Monday afternoon? Senator Weicker has indicated he will be supportive of our efforts to see that there is funding for a center where people can get not only the information we have outlined, but additional referral, where to go, where treatment is available, where testing is available. Also tying it into the local resources. Would you be able to do that for us?

Dr. HOPKINS. Certainly.

Senator D'AMATO. I would also like to know more about AIDS' dormancy period. Over what period of time may someone have the disease and not know it. Some may indeed have the disease and be carriers, but somewhat dormant. Some people have said 2 years. I have heard estimates of 5 years. It has even been estimated as high as 7 years. Do we have any information on this?

Dr. MASON. Let me start off and then my colleagues may want to add more. This is a new disease and we are gaining information at a tremendous rate. I don't think ever before in the history of a disease has so much information become available in such a short period of time. We are learning every day. Just to illustrate, in one study that has been performed with 35 homosexual male clinic patients in San Francisco, many blood specimens have been drawn over time. In this study the serum had just been stored and could be analyzed with the new AIDS test. It was shown in 1980 that 31 of this group were positive for antibodies to HTLV-III/LAV.

So 5 years later, you could find the 31 people and see if they were still alive and what their circumstances were. When CDC went back and identified those 31, they found that all 31 were living 5 years later in 1985. Two of the 31 have classical AIDS with all of the symptoms; only a few more have generalized lymphadenopathy—was it 6 or 8?

Dr. HOPKINS. Eight.

Dr. MASON. Eight additional had what is called AIDS-related complex, generalized changes in their bloodstream. Of the 31, 21 5 years later are still asymptomatic for AIDS.

Senator D'AMATO. Yes; but, doctor, let me just say this to you. What you are saying is that 30 percent—30 percent—had either AIDS, two of them with classical AIDS, which is almost 10 percent, the other eight showed severe problems, AIDS-related kinds of diseases. When you take this figure and understand it as 30 percent, let me tell you to this unscientifically as I am not trained in this area—I barely passed biology—that this sounds like we had better get a handle on what it is when somebody has the antibodies. That raises another question.

We are doing these tests at the blood banks. I understand in certain areas, and I don't know if this is true, that when tests are done to determine the existence of an antibody, positive for AIDS, people are not being informed. They won't take their blood, but they don't inform them either. Should the people be informed that they have the antibody? Should we then be conducting followup tests? How long does it take to do this test? Is it a finger prick with immediate indications either way?

Dr. MASON. I am going to ask Dr. Young to give you the answers on your questions about the blood bank, what happens there and how long it takes to do the test and the followup.

Dr. YOUNG. Senator, I appreciate your concern and also being a native of New York, I understand fully the concerns that you have for our State and the individuals throughout the country. The antibody test that is performed is a very rapid test. It is not a test of days. It is a test of hours, and it is a test that is highly sensitive and is able to detect antibodies to HTLV-III virus within the blood supply. As we said the tests in motion, the goal is to screen blood so that blood that was potentially dangerous could be removed from the blood supply. Therefore, the test sets an overly high level of sensitivity. We felt that if we should err, we should err on the side of removing blood that was questionable rather than the other way.

Senator D'AMATO. Absolutely. I agree.

Dr. YOUNG. Therefore, in that sense, in the population that is not at high risk, in two out of every three of the tests on followup we'll find there may be some of the factors that give rise to the the positivity. Thus, we require in our guidelines that after the first ELISA test, that a second ELISA test is done to confirm whether or not the blood is positive. We also recommend that there are other tests, and this is a western blot, that can more specifically determine the positivity and whether it is specifically related to antibodies to the virus, since antibodies can also be present to the tissue culture cells that may be used to grow the virus.

A single test in itself is not sufficient to establish the disease, even a repeat positive. Thus, we recommend that a person have the consultation of a physician which comes to the very heart of your question. It is our recommendation that local communities take into consideration the exclusion of the individual blood from the blood supply and then after that test has been confirmed, again depending on the local circumstances, that the individual be informed and asked to seek a physician's further counsel. But the test in and of itself is only one piece of the information. There is a lot of local discretion. There is some variability from community to community and we are now working on the more formal regulations to see what would be the best ways to proceed.

Senator D'AMATO. You see why it can be very easily developed. I think there is a big unknown out there.

Dr. YOUNG. There is a big unknown.

Senator D'AMATO. I think the most unfortunate victims are the infants born into this, and the tragic cases of people who develop AIDS through the blood transfusions. A little boy comes down with it or a youngster comes down with it, through no fault of their own.

Dr. YOUNG. Absolutely, that is why we put the highest priority on ensuring the safety of the blood supply.

Senator D'AMATO. It seems to me regarding procedure to follow up on those who show indications of having a positive virus for AIDS, that further work needs to be done. What about cases in the military? It seems to me, again, that this should be an area of concern. If the test is easy, why shouldn't it be administered within the military if you see a necessity for that?

Dr. YOUNG. The test as it was developed, Senator, was developed as a screening test for blood and plasma. It was not developed as a test to diagnose HTLV-III infection. Thus, it has to be looked at in this case through the best medical advice to determine if at all it would be applicable to any further purposes.

I would like to add two other points I did not answer to your earlier question. First, part of the FDA's effort is to answer the exact question you asked. What happens to a person who is antibody positive? There are studies, fortunately, provided through the budgets we receive to look at the subsequent fate of positivity. We are also looking at other tests——

Senator D'AMATO. Can you give us any further information regarding AIDS dormancy period than the example of the 31 individuals you mentioned earlier? Does that concern you, when you have 31 individuals, of which 2 indicated they had AIDS and 8 others revealed related symptoms? It appears as though we need movement in that area.

Dr. YOUNG. Let me try to answer that and then ask Dr. Mason whose field of expertise is in epidemiology. The concern is certainly there. The best indication that we have, though, is on the plasma or blood samples from individuals 5 or 6 years ago. I just approved the test in March, we really don't have a big backlog of the blood test coming through the Red Cross. We are desperately interested in, and CDC is working with the blood community in Atlanta, to also try to determine what positivity means. We want to know, first, what the real epidemiological factors are and then develop the chemotherapeutic agents and the immune-stimulating entities to counteract it. Dr. Mason can probably add further from an epidemiological standpoint.

Dr. MASON. Let me return to the 31 individuals and say this is a very small sample. The point we want to make is that those who are still well, the 21, have no symptoms. You asked about the incubation period, and we generally say that this is a disease with a very long incubation period. Few adults have an incubation period shorter than 1 year, and we don't know but what the 21 are still incubating the disease. Until we can follow these infected individuals for second and third 5-year periods, we really won't know how long the incubation period might be. We also need to do these studies on much larger groups because 31 doesn't give us enough information to generalize to the whole population. It does show we have a lot of infected people in the United States who are not today classified as AIDS cases because they have AIDS-related complex and an even larger group that are infected but without any symptoms.

Senator D'AMATO. Thank you very much. Thank you, Mr. Chairman.

Senator WEICKER. I have a question which I am going to ask. Before I do, Dr. Lenfant, do you have any further comment on Senator D'Amato's situation, as responded to by Dr. Mason and Dr. Young.

Dr. LENFANT. As you know, Mr. Chairman, in our study of a general population, we collected samples from 200,000 blood donors. At the present time we are testing the blood samples for the HTLV–III antibody, using the assay which is now available. I expect that in a few months from now, we will have a picture of the rate of HTLV–III antibody positivity from a general population which gives blood on a voluntary basis. But again these data will not be available before a few months from now.

Senator WEICKER. Thank you very much. The question asked through the Chair is from Nicholas Benton of Intercontinental Media. The question consists of two parts. If no casual contact risk, if, one, how do you account for the high levels of heterosexual transmission of AIDS in Africa? That is the first part.

Dr. MASON. There are various definitions of heterosexual transmission. When we talk of heterosexual transmission, we mean transmission between a man and a woman or a woman and a man through sexual intercourse or other sexual practice. There is no question but what a man with AIDS or a man who is AIDS antibody test positive, even though they have no symptoms, can transmit the disease to a woman. That has been very clearly demonstrated in our studies of hemophiliacs. These men who were infected through the clotting factors, then, can infect their wives.

The evidence in the United States for infection from women to men is not as clearcut. But, as we published in the "Morbidity and Mortality Weekly Report" 1 week ago, there are 15 cases where you cannot identify any risk factors other than sexual contact with a positive woman. One has to assume, to be prudent, that women can transmit the disease sexually to men. The disease goes bidirectionally from men to women and women to men, probably not moving well from women to men here in the United States. This is heterosexual transmission.

This differs from so-called casual transmission. When there is one infected child and one uninfected child in a home, does transmission ever occur between those two? We find it does not, even though the children eat at the same table, share common kitchen utensils, or even share the same bed. That kind of casual transmission, and through sneezing, coughing, et cetera isn't occurring. Heterosexual transmission is transmission through a sexual act. We see those as two very different kinds of contact. Sexual transmission heterosexually, yes. Casual transmission between children or adults, no.

Senator WEICKER. The second part of the question is what about potential virus mutation into stronger forms with better survivability?

Dr. LENFANT. Can I turn that over to Dr. Wyngaarden?

Dr. WYNGAARDEN. Dr. DeVita?

Dr. DEVITA. The virus does, in fact, come in many coats. There are at least 100 isolates of the virus. It does have different coats. That is the bad news.

The good news is the viral of any of these don't seem to differ significantly and some of the work that we are doing now, trying to prepare antibodies, indicates we may be able to develop antibodies on portions of the envelope of the virus.

It is somewhat of a problem, but not a significant problem.

Senator WEICKER. I just want to make sure Senator D'Amato has no further questions. I have other questions for submission to the record.

I want to thank all of you gentlemen for your appearance before us.

Is there anything any of you care to state that I haven't touched upon or you haven't touched upon in your testimony?

Senator D'AMATO. Mr. Chairman, I have one question.

Dr. Kenneth Mayer from Brown University has indicated a linkage with respect to nitrates in AIDS, not the intravenous or the blood kinds of transfers that we think generally about.

Have you conducted any studies in this area? In other words, in terms of the utilization of paraphernalia, what effect has drug use itself had in the spread of AIDS, as opposed to simply the use of intravenous devices, needles, et cetera, in contaminating blood from one to another?

Dr. MASON. Are you referring to amyl nitrates?

Senator D'AMATO. Amyl nitrates, he says. He raises the question as to whether or not there is a direct correlation and linkage between drug use, et cetera.

Dr. MASON. Early in this epidemic, it was reported that there seemed to be a lot of people with AIDS who had used amyl nitrate. Therefore, in the early epidemological studies, association with this was carefully looked at to see if there was a cause and effect relationship. It was subsequently ruled out as a cause of AIDS. There is no question that this virus that we have talked about, HTLV–III, is the cause of AIDS.

Now, whether other substances or cofactors may in some way make the person more susceptible to the clinical aspects of the disease after the virus has been transmitted to them, is being looked into. For example, we know that with other infectious diseases, people who are poorly nourished tend to get more severe infections.

In other words, are there other influences on the course of the disease after infection with the virus? Intense research is being carried out at this time to look at substances, such as marijuana, amyl nitrate, and other viruses. If you already have hepatitis-B and then get AIDS, is the disease more rapidly progressing?

Senator D'AMATO. That goes along with the reports that a higher percentage of AIDS victims in New York, it would seem, tend to contract pneumonia, those who are using drugs, involved in drug abuse, while those in San Francisco come down with a form of cancer.

Dr. MASON. Kaposi's sarcoma. You are absolutely right, these may affect the course of the disease but without the virus, you don't get the disease. Whether other substances or other infections may enhance the progress of disease, is part of studies ADAMHA, CDC, NIH, and others are doing. We want to identify any factors that may influence or affect the course of the disease after the infection. I don't think we have any good data at this point in time.

Dr. YOUNG. I agree with what you have said, Jim. The question is a very important and perceptive one. The insidious part of this disease is it attacks the immune system. We don't know yet what might cause the proliferation of the immune system, lymphocytes, that might make them more susceptible to infection.

I know there is a great interest in that. We have been working closely at FDA under the leadership of Dr. Myer to look at cofactors. I think it is important to emphasize this is a disease we have really just seen since the early 1980's and there will be a lot of facts and information and we are working very hard to see if we can get a full picture of the disease.

Senator D'AMATO. Dr. Macdonald?

Dr. MACDONALD. It is a good question, Senator, and one we are looking at seriously, relative to the relationship of butyl nitrate and other drugs of abuse. One of the things which interested me in visiting AIDS treatment programs at Memorial Sloan-Kettering, is the different disease pattern that occurs in the IV drug user and the person who gets AIDS from sexual contact.

At Sloan-Kettering, the average survival time for the homosexual with AIDS is 17 months. That is more than twice as long as the IV drug user who dies, on average, in 7 months. More importantly, the IV drug users die with different diseases.

Kaposi's sarcoma is more common in the homosexual while the opportunistic infections tend to cluster in the drug user. Amyl nitrate is more commonly used in the homosexual community. They use it for sexual purposes. We are looking at that very, very seriously. It is an important part of the cofactor research.

Dr. WYNGAARDEN. Senator, an important part of the epidemiological studies that are ongoing and proposed in the international arena address that question of different cofactors. For example, the sex ratio of the disease in Africa is approximately 50–50. It is quite different from the United States. One of the things being asked is "Are the cofactors different in that locality?"

Senator D'AMATO. Thank you, very much, Mr. Chairman.

Senator WEICKER. Gentlemen, thank you very much.

There is a vote on at the present time. What I would like to do is introduce the next panel, have them take their seats and we will be right back after the vote.

Next we will hear from Dr. William Haseltine of Harvard University; Dr. Malcolm A.S. Moore of Memorial Sloan-Kettering Cancer Center and Dr. Don C. Des Jarlais, New York State Division of Substance Abuse.

Specifically, these gentlemen represent the scientific community and will respond to questions of what should be done.

I would gather in the course of this testimony, we will hear further opinions, new opinions and very much looking forward to the testimony of all concerned.

Having introduced the panel, I will now declare a short 5-minute recess during which time Senator D'Amato and myself will vote and then we will commence with the testimony of Dr. Haseltine.

[A brief recess was taken.]

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

There will be some additional questions from myself and other members of the subcommittee which we will submit to each agency for their response.

[The following questions were not asked at the hearing but were submitted to be answered for the record:]

OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH

Questions Submitted by the Subcommittee

Question: How contagious is AIDS and how can be it be transmitted?

Answer: Casual contact with AIDS patients or persons who might be at risk for the illness does not place others at risk for getting the illness. No cases have been found in which AIDS has been transmitted by casual household contact with AIDS patients or with persons in high risk groups. Further, while the AIDS virus, HTLV-III, has been found in saliva and tears, there have been no cases reported in which exposure to either was shown to result in transmission. We have not received any reports in which ambulance drivers, police, and firefighters who have assisted AIDS patients have become ill with the disease. There has not been a case of AIDS or infection with HTLV-III reported to us in nurses, doctors, and health-care personnel as a result of caring for AIDS patients, other than through needle stick injury.

However, health care and laboratory workers should follow safety procedures carefully when handling any blood and tissue samples from patients with potentially transmissible diseases, including AIDS.

AIDS is spread by sexual contact; sharing of needles among IV drug abusers and infected mothers transmitting the virus to their babies across the placenta and, likely, through breast milk. While the risk for transmission of HTLV-III through transfusion of blood or blood products was never great, it has been virtually eliminated through new methods of screening the blood supply. The risk of getting AIDS is probably increased by having multiple sexual partners, either homosexual or heterosexual, and sharing of needles among those using illicit drugs.

Question: Is there any evidence at all that indicates AIDS has been transmitted casually, by sneezing, coughing, or other non-intimate means?

Answer: There is no evidence that HTLV-III has been transmitted casually, by sneezing, coughing or other non-intimate means. Casual contact with AIDS patients or individuals who might be at risk for the illness does not place others at risk for getting the illness. In studies of over 300 households with AIDS patients, not one person -- other than a sexual contact or a child born to an infected mother -- has become infected with HTLV-III or developed AIDS.

In studies of more than 1,758 health-care workers who have close contact with very ill, often hospitalized, AIDS patients, not one has developed AIDS or become infected with HTLV-III as a result of contact with patients, other than through needle stick injury. Twenty-six health-care workers have had positive test results. Of these twenty-six, all but three belonged to risk groups. Epidemiologic information is not available for one of these three health-care workers. The other two suffered needle stick injuries, and we continue to strongly urge people handling needles to observe the precautions that the Public Health Service published in the November 5, 1982, issue of the Center for Disease Control's (CDC), Morbidity and Mortality Weekly Report (MMWR) (Attachment I).

ATTACHMENT 1

Current Trends

Acquired Immune Deficiency Syndrome (AIDS): Precautions for Clinical and Laboratory Staffs

The etiology of the underlying immune deficiencies seen in AIDS cases is unknown. One hypothesis consistent with current observations is that a transmissible agent may be involved. If so, transmission of the agent would appear most commonly to require intimate, direct contact involving mucosal surfaces, such as sexual contact among homosexual males, or through parenteral spread, such as occurs among intravenous drug abusers and possibly hemophilia patients using Factor VIII products. Airborne spread and interpersonal spread through casual contact do not seem likely. These patterns resemble the distribution of disease and modes of spread of hepatitis B virus, and hepatitis B virus infections occur very frequently among AIDS cases.

There is presently no evidence of AIDS transmission to hospital personnel from contact with affected patients or clinical specimens. Because of concern about a possible transmissible agent, however, interim suggestions are appropriate to guide patient-care and laboratory personnel, including those whose work involves experimental animals. At present, it appears prudent for hospital personnel to use the same precautions when caring for patients with AIDS as those used for patients with hepatitis B virus infection, in which blood and body fluids likely to have been contaminated with blood are considered infective. Specifically, patient-care and laboratory personnel should take precautions to avoid direct contact of skin and mucous membranes with blood, blood products, excretions, secretions, and tissues of persons judged likely to have AIDS. The following precautions do not specifically address outpatient care, dental care, surgery, necropsy, or hemodialysis of AIDS patients. In general, procedures appropriate for patients known to be infected with hepatitis B virus are advised, and blood and organs of AIDS patients should not be donated.

The precautions that follow are advised for persons and specimens from persons with: opportunistic infections that are not associated with underlying immunosuppressive disease or therapy; Kaposi's sarcoma (patients under 60 years of age); chronic generalized lymphadenopathy, unexplained weight loss and/or prolonged unexplained fever in persons who belong to groups with apparently increased risks of AIDS (homosexual males, intravenous drug abusers, Haitian entrants, hemophiliacs); and possible AIDS (hospitalized for evaluation). Hospitals and laboratories should adapt the following suggested precautions to their individual circumstances; these recommendations are not meant to restrict hospitals from implementing additional precautions.

A. The following precautions are advised in providing care to AIDS patients:

1. Extraordinary care must be taken to avoid accidental wounds from sharp instruments contaminated with potentially infectious material and to avoid contact of open skin lesions with material from AIDS patients.

2. Gloves should be worn when handling blood specimens, blood-soiled items, body fluids, excretions, and secretions, as well as surfaces, materials, and objects exposed to them.
3. Gowns should be worn when clothing may be soiled with body fluids, blood, secretions, or excretions.
4. Hands should be washed after removing gowns and gloves and before leaving the rooms of known or suspected AIDS patients. Hands should also be washed thoroughly and immediately if they become contaminated with blood.
5. Blood and other specimens should be labeled prominently with a special warning, such as "Blood Precautions" or "AIDS Precautions." If the outside of the specimen container is visibly contaminated with blood, it should be cleaned with a disinfectant (such as a 1:10 dilution of 5.25% sodium hypochlorite [household bleach] with water). All blood specimens should be placed in a second container, such as an impervious bag, for transport. The container or bag should be examined carefully for leaks or cracks.
6. Blood spills should be cleaned up promptly with a disinfectant solution, such as sodium hypochlorite (see above).
7. Articles soiled with blood should be placed in an impervious bag prominently labeled "AIDS Precautions" or "Blood Precautions" before being sent for reprocessing or disposal. Alternatively, such contaminated items may be placed in plastic bags of a particular color designated solely for disposal of infectious wastes by the hospital. Disposable items should be incinerated or disposed of in accord with the hospital's policies for disposal of infectious wastes. Reusable items should be reprocessed in accord with hospital policies for hepatitis B virus-contaminated items. Lensed instruments should be sterilized after use on AIDS patients.
8. Needles should not be bent after use, but should be promptly placed in a puncture-resistant container used solely for such disposal. Needles should not be reinserted into their original sheaths before being discarded into the container, since this is a common cause of needle injury.
9. Disposable syringes and needles are preferred. Only needle-locking syringes or one-piece needle-syringe units should be used to aspirate fluids from patients, so that collected fluid can be safely discharged through the needle, if desired. If reusable syringes are employed, they should be decontaminated before reprocessing.
10. A private room is indicated for patients who are too ill to use good hygiene, such as those with profuse diarrhea, fecal incontinence, or altered behavior secondary to central nervous system infections.

Precautions appropriate for particular infections that concurrently occur in AIDS patients should be added to the above, if needed.

B. The following precautions are advised for persons performing laboratory tests or studies on clinical specimens or other potentially infectious materials (such as inoculated tissue cultures, embryonated eggs, animal tissues, etc.) from known or suspected AIDS cases:

1. Mechanical pipetting devices should be used for the manipulation of all liquids in the laboratory. Mouth pipetting should not be allowed.
2. Needles and syringes should be handled as stipulated in Section A (above).
3. Laboratory coats, gowns, or uniforms should be worn while working with potentially infectious materials and should be discarded appropriately before leaving the laboratory.
4. Gloves should be worn to avoid skin contact with blood, specimens containing blood, blood-soiled items, body fluids, excretions, and secretions, as well as surfaces, materials, and objects exposed to them.
5. All procedures and manipulations of potentially infectious material should be performed carefully to minimize the creation of droplets and aerosols.
6. Biological safety cabinets (Class I or II) and other primary containment devices (e.g., centrifuge safety cups) are advised whenever procedures are conducted that have a high potential for creating aerosols or infectious droplets. These include centrifuging, blending, sonicating, vigorous mixing, and harvesting infected tissues from animals or embryonated eggs. Fluorescent activated cell sorters generate droplets that could potentially result in infectious aerosols. Translucent plastic shielding between the droplet-collecting area and the equipment operator should be used to reduce the presently uncer-

tain magnitude of this risk. Primary containment devices are also used in handling materials that might contain concentrated infectious agents or organisms in greater quantities than expected in clinical specimens.

7. Laboratory work surfaces should be decontaminated with a disinfectant, such as sodium hypochlorite solution (see A5 above), following any spill of potentially infectious material and at the completion of work activities.
8. All potentially contaminated materials used in laboratory tests should be decontaminated, preferably by autoclaving, before disposal or reprocessing.
9. All personnel should wash their hands following completion of laboratory activities, removal of protective clothing, and before leaving the laboratory.

C. The following additional precautions are advised for studies involving experimental animals inoculated with tissues or other potentially infectious materials from individuals with known or suspected AIDS.

1. Laboratory coats, gowns, or uniforms should be worn by personnel entering rooms housing inoculated animals. Certain nonhuman primates, such as chimpanzees, are prone to throw excreta and to spit at attendants; personnel attending inoculated animals should wear molded surgical masks and goggles or other equipment sufficient to prevent potentially infective droplets from reaching the mucosal surfaces of their mouths, nares, and eyes. In addition, when handled, other animals may disturb excreta in their bedding. Therefore, the above precautions should be taken when handling them.
2. Personnel should wear gloves for all activities involving direct contact with experimental animals and their bedding and cages. Such manipulations should be performed carefully to minimize the creation of aerosols and droplets.
3. Necropsy of experimental animals should be conducted by personnel wearing gowns and gloves. If procedures generating aerosols are performed, masks and goggles should be worn.
4. Extraordinary care must be taken to avoid accidental sticks or cuts with sharp instruments contaminated with body fluids or tissues of experimental animals inoculated with material from AIDS patients.
5. Animal cages should be decontaminated, preferably by autoclaving, before they are cleaned and washed.
6. Only needle-locking syringes or one-piece needle-syringe units should be used to inject potentially infectious fluids into experimental animals.

The above precautions are intended to apply to both clinical and research laboratories. Biological safety cabinets and other safety equipment may not be generally available in clinical laboratories. Assistance should be sought from a microbiology laboratory, as needed, to assure containment facilities are adequate to permit laboratory tests to be conducted safely.

Reported by Hospital Infections Program, Div of Viral Diseases, Div of Host Factors, Div of Hepatitis and Viral Enteritis, AIDS Activity, Center for Infectious Diseases, Office of Biosafety, CDC; Div of Safety, National Institutes of Health.

Question: Has the Department taken an official position on how children, health-care workers, food handlers and others with AIDS should be accepted in schools, hospitals or other workplaces?

Answer: The Department has taken an official position on how children should be accepted into school. We have recently published recommendations on how children infected with HTLV-III should be dealt with in schools and foster care settings. In general, after proper screening, most infected school-age children should be allowed to attend school and after-school day care. But pre-school children and mentally retarded children present a risk to others where accidental transfer of body fluids is a possibility. In such cases, a more restricted environment is advised until more is known about transmission. The recommendations were published in the August 30, 1985, issue of the MMWR (Attachment II).

ATTACHMENT 2

Current Trends

Education and Foster Care of Children Infected with Human T-Lymphotropic Virus Type III/ Lymphadenopathy-Associated Virus

The information and recommendations contained in this document were developed and compiled by CDC in consultation with individuals appointed by their organizations to represent the Conference of State and Territorial Epidemiologists, the Association of State and Territorial Health Officers, the National Association of County Health Officers, the Division of Maternal and Child Health (Health Resources and Services Administration), the National Association for Elementary School Principals, the National Association of State School Nurse Consultants, the National Congress of Parents and Teachers, and the Children's Aid Society. The consultants also included the mother of a child with acquired immunodeficiency syndrome (AIDS), a legal advisor to a state education department, and several pediatricians who are experts in the field of pediatric AIDS. This document is made available to assist state and local health and education departments in developing guidelines for their particular situations and locations.

These recommendations apply to all children known to be infected with human T-lymphotropic virus type III/lymphadenopathy-associated virus (HTLV-III/LAV). This includes children with AIDS as defined for reporting purposes (Table 1); children who are diagnosed by their physicians as having an illness due to infection with HTLV-III/LAV but who do not meet the case definition; and children who are asymptomatic but have virologic or serologic evidence of infection with HTLV-III/LAV. These recommendations do not apply to siblings of infected children unless they are also infected.

BACKGROUND

The Scope of the Problem. As of August 20, 1985, 183 of the 12,599 reported cases of AIDS in the United States were among children under 18 years of age. This number is expected to double in the next year. Children with AIDS have been reported from 23 states, the District of Columbia, and Puerto Rico, with 75% residing in New York, California, Florida, and New Jersey.

The 183 AIDS patients reported to CDC represent only the most severe form of HTLV-III/LAV infection, i.e., those children who develop opportunistic infections or malignancies (Table 1). As in adults with HTLV-III/LAV infection, many infected children may have milder illness or may be asymptomatic.

Legal Issues. Among the legal issues to be considered in forming guidelines for the education and foster care of HTLV-III/LAV-infected children are the civil rights aspects of public school attendance, the protections for handicapped children under 20 U.S.C. 1401 et seq. and 29 U.S.C. 794, the confidentiality of a student's school record under state laws and under 20 U.S.C. 1232g, and employee right-to-know statutes for public employees in some states.

Confidentiality Issues. The diagnosis of AIDS or associated illnesses evokes much fear from others in contact with the patient and may evoke suspicion of life styles that may not be acceptable to some persons. Parents of HTLV-III/LAV-infected children should be aware of the potential for social isolation should the child's condition become known to others in the care or educational setting. School, day-care, and social service personnel and others involved in educating and caring for these children should be sensitive to the need for confidentiality and the right to privacy in these cases.

TABLE 1. Provisional case definition for acquired immunodeficiency syndrome (AIDS) surveillance of children

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For the limited purposes of epidemiologic surveillance, CDC defines a case of pediatric acquired immunodeficiency syndrome (AIDS) as a child who has had

1. A reliably diagnosed disease at least moderately indicative of underlying cellular immunodeficiency, and
2. No known cause of underlying cellular immunodeficiency or any other reduced resistance reported to be associated with that disease.

The diseases accepted as sufficiently indicative of underlying cellular immunodeficiency are the same as those used in defining AIDS in adults. In the absence of these opportunistic diseases, a histologically confirmed diagnosis of chronic lymphoid interstitial pneumonitis will be considered indicative of AIDS unless test(s) for HTLV-III/LAV are negative. Congenital infections, e.g., toxoplasmosis or herpes simplex virus infection in the first month after birth or cytomegalovirus infection in the first 6 months after birth must be exluded.

Specific conditions that must be excluded in a child are:

1. Primary immunodeficiency diseases—severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia, graft versus host disease, neutropenia, neutrophil function abnormality, agammaglobulinemia, or hypogammaglobulinemia with raised IgM.
2. Secondary immunodeficiency associated with immunosuppressive therapy, lymphoreticular malignancy, or starvation.

ASSESSMENT OF RISKS

Risk Factors for Acquiring HTLV-III/LAV Infection and Transmission. In adults and adolescents, HLTV-III/LAV is transmitted primarily through sexual contact (homosexual or heterosexual) and through parenteral exposure to infected blood or blood products. HTLV-III/LAV has been isolated from blood, semen, saliva, and tears but transmission has not been documented from saliva and tears. Adults at increased risk for acquiring HTLV-III/LAV include homosexual/bisexual men, intravenous drug abusers, persons transfused with contaminated blood or blood products, and sexual contacts of persons with HTLV-III/LAV infection or in groups at increased risk for infection.

The majority of infected children acquire the virus from their infected mothers in the perinatal period (*1-4*). In utero or intrapartum transmission are likely, and one child reported from Australia apparently acquired the virus postnatally, possibly from ingestion of breast milk (*5*). Children may also become infected through transfusion of blood or blood products that contain the virus. Seventy percent of the pediatric cases reported to CDC occurred among children whose parent had AIDS or was a member of a group at increased risk of acquiring HTLV-III/LAV infection, 20% of the cases occurred among children who had received blood or blood products, and for 10%, investigations are incomplete.

Risk of Transmission in the School, Day-Care or Foster-Care Setting. None of the identified cases of HTLV-III/LAV infection in the United States are known to have been transmitted in the school, day-care, or foster-care setting or through other casual person-to-person contact. Other than the sexual partners of HTLV-III/LAV-infected patients and infants born to infected mothers, none of the family members of the over 12,000 AIDS patients reported to CDC have been reported to have AIDS. Six studies of family members of patients with HTLV-III/LAV infection have failed to demonstrate HTLV-III/LAV transmission to adults who were not sexual contacts of the infected patients or to older children who were not likely at risk from perinatal transmission (*6-11*).

Based on current evidence, casual person-to-person contact as would occur among schoolchildren appears to pose no risk. However, studies of the risk of transmission through contact between younger children and neurologically handicapped children who lack control of their body secretions are very limited. Based on experience with other communicable diseases, a theoretical potential for transmission would be greatest among these children. It should be emphasized that any theoretical transmission would most likely involve exposure of open skin lesions or mucous membranes to blood and possibly other body fluids of an infected person.

Risks to the Child with HTLV-III/LAV Infection. HTLV-III/LAV infection may result in immunodeficiency. Such children may have a greater risk of encountering infectious agents in a school or day-care setting than at home. Foster homes with multiple children may also increase the risk. In addition, younger children and neurologically handicapped children who may display behaviors such as mouthing of toys would be expected to be at greater risk for acquiring infections. Immunodepressed children are also at greater risk of suffering severe complications from such infections as chickenpox, cytomegalovirus, tuberculosis, herpes simplex, and measles. Assessment of the risk to the immunodepressed child is best made by the child's physician who is aware of the child's immune status. The risk of acquiring some infections, such as chickenpox, may be reduced by prompt use of specific immune globulin following a known exposure.

RECOMMENDATIONS

1. Decisions regarding the type of educational and care setting for HTLV-III/LAV-infected children should be based on the behavior, neurologic development, and physical condition of the child and the expected type of interaction with others in that setting. These decisions are best made using the team approach including the child's physician, public health personnel, the child's parent or guardian, and personnel associated with the proposed care or educational setting. In each case, risks and benefits to both the infected child and to others in the setting should be weighed.
2. For most infected school-aged children, the benefits of an unrestricted setting would outweigh the risks of their acquiring potentially harmful infections in the setting and the apparent nonexistent risk of transmission of HTLV-III/LAV. These children should be allowed to attend school and after-school day-care and to be placed in a foster home in an unrestricted setting.
3. For the infected preschool-aged child and for some neurologically handicapped children who lack control of their body secretions or who display behavior, such as biting, and those children who have uncoverable, oozing lesions, a more restricted environment is advisable until more is known about transmission in these settings. Children infected with HTLV-III/LAV should be cared for and educated in settings that minimize exposure of other children to blood or body fluids.
4. Care involving exposure to the infected child's body fluids and excrement, such as feeding and diaper changing, should be performed by persons who are aware of the child's HTLV-III/LAV infection and the modes of possible transmission. In any setting involving an HTLV-III/LAV-infected person, good handwashing after exposure to blood and body fluids and before caring for another child should be observed, and gloves should be worn if open lesions are present on the caretaker's hands. Any open lesions on the infected person should also be covered.
5. Because other infections in addition to HTLV-III/LAV can be present in blood or body fluids, all schools and day-care facilities, regardless of whether children with HTLV-III/LAV infection are attending, should adopt routine procedures for handling blood or body fluids. Soiled surfaces should be promptly cleaned with disinfectants, such as household bleach (diluted 1 part bleach to 10 parts water). Disposable towels or tissues should be used whenever possible, and mops should be rinsed in the disinfectant. Those who are cleaning should avoid exposure of open skin lesions or mucous membranes to the blood or body fluids.
6. The hygienic practices of children with HTLV-III/LAV infection may improve as the child matures. Alternatively, the hygienic practices may deteriorate if the child's condition worsens. Evaluation to assess the need for a restricted environment should be performed regularly.
7. Physicians caring for children born to mothers with AIDS or at increased risk of acquiring HTLV-III/LAV infection should consider testing the children for evidence of HTLV-III/LAV infection for medical reasons. For example, vaccination of infected children with live virus vaccines, such as the measles-mumps-rubella vaccine (MMR), may be hazardous. These children also need to be followed closely for problems with growth and development and given prompt and aggressive therapy for infections and exposure to potentially lethal infections, such as varicella. In the event that an antiviral agent or other therapy for HTLV-III/LAV infection becomes available, these children should be considered for such therapy. Knowledge that a child is infected will allow parents and other caretakers to take precautions when exposed to the blood and body fluids of the child.

8. Adoption and foster-care agencies should consider adding HTLV-III/LAV screening to their routine medical evaluations of children at increased risk of infection before placement in the foster or adoptive home, since these parents must make decisions regarding the medical care of the child and must consider the possible social and psychological effects on their families.
9. Mandatory screening as a condition for school entry is not warranted based on available data.
10. Persons involved in the care and education of HTLV-III/LAV-infected children should respect the child's right to privacy, including maintaining confidential records. The number of personnel who are aware of the child's condition should be kept at a minimum needed to assure proper care of the child and to detect situations where the potential for transmission may increase (e.g., bleeding injury).
11. All educational and public health departments, regardless of whether HTLV-III/LAV-infected children are involved, are strongly encouraged to inform parents, children, and educators regarding HTLV-III/LAV and its transmission. Such education would greatly assist efforts to provide the best care and education for infected children while minimizing the risk of transmission to others.

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The Department is developing guidelines dealing with occupational issues concerning persons infected with HTLV-III. These guidelines will be published soon in the MMWR.

Question: What efforts is the Department making to inform medical professionals, school officials, and the public about research developments resulting from NIH, CDC, and ADAMHA studies?

Answer: In order to promote widespread awareness and prevention of AIDS and other HTLV-III infections, all Public Health Service (PHS) agencies have been participating in the national effort to provide information to the scientific and public health communities, members of risk groups, and the public. The Department has recently accelerated its public information and education activities to advise Americans of the current information about transmissibility of the disease and the behavioral changes they can make to protect themselves and their loved ones. The Public Health Service Plan for the Prevention and Control of Acquired Immune Deficiency Syndrome (AIDS) recently published in the September-October 1985 issue of Public Health Reports outlines these efforts (Attachment III).

ATTACHMENT 3

ARTICLES—POLICY

Public Health Service Plan for the Prevention and Control of Acquired Immune Deficiency Syndrome (AIDS)

Foreword

The PHS Executive Task Force on AIDS has developed this framework within which the Public Health Service is working to control and prevent acquired immune deficiency syndrome (AIDS) by the year 2,000. Our comprehensive plan is based on the state of the art since the isolation of the human T Lymphotropic Virus-III and development of the blood test to detect evidence of infection by the virus.

The plan includes broad-scale information and education activities in addition to research efforts to develop a vaccine, and treatments to fight the AIDS virus and restore functioning of the immune system.

Within each of these areas the PHS agencies have developed comprehensive plans of action. Programs to effect behavior changes for persons at risk and provision of up-to-date information on AIDS are important features of the plan, which assumes that a vaccine and effective therapy may not be immediately available. This outline and the specific plans of action are dynamic—as new information becomes available, steps will be modified accordingly.

The plan was developed as a continuation of the Public Health Service's extraordinary efforts to deal with this tragic disease almost since the first cases were reported in 1981.

James O. Mason, MD, DrPH
Acting Assistant Secretary for Health

PURPOSE:

This document provides an outline for the key goals and objectives that must be met to achieve prevention and control of AIDS. The plan calls for action by Federal agencies, State and local health departments, professional organizations, and volunteer groups. Many of the specific objectives cannot be expressed in measurable terms because of inadequate current information, but they are included here even though modifications will be made as more data are generated.

I. PROBLEM:

A. AIDS is a very serious, often fatal, disease caused by the virus HTLV-III.
B. The incidence of AIDS and infection with HTLV-III is increasing steadily in the United States.
C. More persons are known to be infected with HTLV-III than have become ill. The incubation period for AIDS in adults may range from 1 to 6 years or more and in infants from 6 months to 5 years or more.
D. Infected persons may be capable of transmitting infection for many years, even though they may remain asymptomatic.
E. The ability of HTLV-III to persist in the infected individual results in a population of persons who may be at risk for years for development of severe illness.
F. HTLV-III infection is transmitted by infected sexual partners through exchange of body fluids, through equipment used to administer intravenous drugs of abuse, through contaminated blood and blood products, and from infected mothers to infants. Members of all population groups thus exposed are at risk.
G. No effective vaccine or therapy exists.

II. ASSUMPTIONS:

A. A person with a repeatedly reactive HTLV-III antibody test is infected with HTLV-III and able to transmit the virus to others.
B. Psychosocial and medical problems will increase as the number of AIDS cases grows and HTLV-III infection spreads.
C. The more HTLV-III infection is disseminated throughout the population before effective control measures begin, the harder it will be to bring it under control.
D. Because there is no means of intervention during the long incubation period to prevent severe AIDS, a vaccine that prevents infection will be an effective tool for control only after it has been in use for several years. On the other hand if early therapy becomes available to reduce infectiousness in those already infected, and if persons at risk take responsible preventive measures, control of AIDS will be realized much sooner.
E. It is unlikely that a vaccine or therapy to substantially limit transmission will be generally available before 1990.
F. Broad scale prevention and control activities, emphasizing educational and information exchange, must begin in the absence of available vaccine and specific therapy. They should be based on current best public health judgment.
G. Demonstration and evaluation projects are needed to determine the efficacy and cost-effectiveness of prevention and control strategies.

III. GOALS:

A. By 1987, reduce increase in transmission of HTLV-III infection.

B. By 1990, reduce increase in the incidence of AIDS.
C. By 2,000, eliminate transmission of HTLV-III infection with a decline in the incidence of AIDS thereafter.

IV. OBJECTIVES:

A. Continue to clarify the epidemiology and natural history of HTLV-III infection.
1. Maintain current epidemiologic surveillance of AIDS cases in the United States.
2. Monitor the incidence of HTLV-III infection by geographic areas and among major high-incidence groups.
3. Define diagnostic criteria for AIDS and other conditions associated with HTLV-III infection.
4. Evaluate the usefulness of surveillance of other AIDS-related conditions.
5. Determine:
a. How frequently and under what circumstances HTLV-III infection persists in an infected individual.
b. The efficiency of virus transmission by route of exposure, magnitude of exposure (dose), and other conditions.
c. The severity of disease in relation to time and source of infection.
d. The time frames for development of antigens and antibodies to HTLV-III in blood of infected individuals.
e. The role of host factors and cofactors, including interaction with other organisms, in disease risk.
6. Develop and evaluate new diagnostic tests for HTLV-III and improve existing assays.
7. In order to clarify risk factors and protective factors for HTLV-III infection and AIDS, conduct epidemiologic investigations in various groups including:
a. Homosexual/bisexual men.
b. IV drug users.
c. Persons with hemophilia.
d. Recipients of units of blood or blood components containing HTLV-III.
e. Both seropositive pregnant women to determine pregnancy outcome and the infants born to them.
f. Heterosexual partners of infected individuals or of those at risk (e.g., prostitutes).
g. Members of households of infected individuals.
h. Health care, dental, and laboratory workers.
i. Populations in countries where AIDS becomes prevalent.

B. Continue to implement national, State, and community risk reduction and education programs as early prevention and control measures.
1. Provide current information on AIDS to all segments of the American public. Special efforts will be made for:
a. Individuals at increased risk for AIDS to effect behavior change, which currently is the only mechanism available to prevent infection.
b. Health care providers to increase diagnostic, treatment, and counseling services.
c. Researchers to increase dissemination of their findings to speed the development of vaccine, therapy, and other intervention measures.
d. Other groups including unions, management, blood collection agencies, high-risk group organizations, and educational authorities to disseminate accurate information to those who may have a responsibility for persons with HTLV-III infection.
2. Develop specific prevention and control recommendations through consensus building among key individuals and groups.
a. Convene representatives of relevant groups and organizations to generate specific recommendations for the control of AIDS among the following groups at high risk:
(1) Homosexual and bisexual men, including representatives of black and Hispanic groups.
(2) IV drug users.
(3) Heterosexual persons with multiple sex partners.
(4) Female partners of men at high risk, with special emphasis on perinatal transmissions.
(5) Haitians and central African entrants to the United States.
(6) Recipients of blood and blood products, organs, and tissues and artificially inseminated women.
b. Convene representatives of State and local government agencies and professional and community groups concerned with research, the provision of care, educational aspects, and psychological aspects of AIDS to assist in coordinating appropriate programs.
3. Encourage the implementation of community risk reduction and health education programs to effect behavior change regarding high-risk sexual practices and the use of IV drugs.
Strong efforts will be especially useful in those geographic areas where high-risk groups do not have high rates of infection.
a. Provide targeted education for groups and individuals at risk regarding specific high-risk behaviors.
b. Provide risk reduction programs for high-risk groups and individuals to enable them to make the needed changes in their behaviors.
4. Provide medical referral and counseling programs to persons who request testing or who know their antibody status as a result of blood or plasma donations.
5. Continue to reduce opportunities for virus transmission through blood and blood products.
a. Encourage voluntary donor deferral.
b. Screen all units of blood and plasma.
c. Require donor deferral lists for persons with reactive tests.
d. Inactivate HTLV-III in all blood components and products where feasible.
6. Encourage testing for donors of organs, tissues, cells, and semen for antibody to HTLV-III.
7. Reduce opportunities for virus transmission through environmental measures.
a. Encourage hospital and laboratory personnel to follow recommended precautions with patients or specimens known or suspected to be HTLV-III positive.
b. Use effective disinfectants on contaminated equipment.
c. Encourage proper personal hygiene among infected persons.

C. Design and evaluate improved prevention and control measures.
1. Develop and evaluate better approaches for detecting infection.
a. Determine antigenic, genetic, and other variation among HTLV-III isolates.
b. Develop and evaluate new antigen tests.
c. Cooperatively develop guidelines for use of currently available and new tests.
2. Develop and evaluate active immunoprophylaxis.
a. Convene scientific advisory committees to plan for development and evaluation of vaccines.
b. Characterize HTLV-III antigens biochemically and structurally to determine the specific component parts of the virus against which the antibodies generated by a vaccine would react.
c. Develop specific candidate vaccines including subunit products, synthetic peptides, genetically synthesized antigens, and others.
d. Develop new means of preparing, packaging, preserving, and transporting vaccine.
e. Develop new, effective methods for delivering vaccine to substantial numbers of people.
3. Develop and evaluate passive immunophylaxis, using artificially prolonged antibody.
4. Develop and evaluate drug and biologic therapy including antivirals, immune stimulants, and combinations of these.

  - a. Evaluate existing candidate compounds in laboratory systems and clinical trials.
  - b. Design, produce, and evaluate new drugs based on results with existing compounds.
  - c. Develop new immune stimulants and test available stimulants in animals or clinical research objects: investigate reconstitution of immune system, e.g., bone marrow transplantation.
  - d. Test immune stimulants combined with antiviral therapy against HTLV-III.
  - e. Evaluate host factors and possible cofactors.
- 5. Develop and improve animal models to accomplish studies that cannot be done with humans or *in vitro* systems.
  - a. Test candidate vaccines and drugs in chimpanzee and rhesus monkeys, which are the only animals shown thus far to be infected with HTLV-III.
  - b. Use existing animal models and seek new species for study of animal retroviruses related to HTLV-III, e.g., feline leukemia in cats and retrovirus infection in nonhuman primates. Study agents that control these viruses.
- 6. Assure that adequate facilities exist to support studies in the development and evaluation of vaccines, antivirals, and immune stimulants listed above.

D. Design and promote prevention and control programs that will enhance effectiveness by incorporating new intervention tools (vaccines/antivirals) as they become available.

Information for medical professionals, school officials, and the public is disseminated via the MMWR, FDA Bulletin, FDA Dear Doctor letters, Public Health Reports, journal articles, bulletins, health pamphlets, medical interviews, national and international conferences, and workshops on AIDS conducted by PHS agencies and attended by outside consultants, organizations and the public. Approximately 40,000 copies of the MMWR -- which has carried 67 articles on AIDS epidemiology, etiology, prevention, and PHS recommendations for high risk groups, precautions for health care workers, and most recently on how children with AIDS should be accepted into school -- are regularly distributed to the health community and published in medical journals.

The national AIDS toll-free hotline (1-800-447-AIDS), or for Atlanta area callers (404-329-1295), is operated by the PHS, and trained professionals answer questions and provide information to any individual who wishes to call. Two press briefings which keep the media abreast of current research developments were recently held: one on September 19, 1985, on heterosexual transmission of AIDS, and one on October 9, 1985, on experimental AIDS therapy. More such briefings are expected. Furthermore, small reference cards, fact sheets, booklets and pamphlets have been designed and distributed to help allay public concerns about AIDS. One of the most widely distributed is Facts about AIDS, updated in August, 1985 (Attachment IV).

ATTACHMENT 4

Facts about AIDS

August 1985

The Acquired Immune Deficiency Syndrome, or AIDS, was first reported in the United States in mid-1981. Since that time, the Public Health Service has received reports of more than 12,000 cases, about 50 percent of which have resulted in death.

AIDS is a serious illness, and a public health problem that merits concern. It has been named the number one priority of the U.S. Public Health Service. Researchers in the Public Health Service and in many major medical institutions have been working for more than four years to study AIDS, identify its cause, and develop treatments and preventive measures.

This fact sheet describes, in question-and-answer form, accurate information about the nature and extent of AIDS, the risk of contracting AIDS, the actions individuals can take to reduce spreading AIDS, and current research and related activities under way in the Public Health Service.

What is AIDS?

AIDS is a serious condition characterized by a defect in natural immunity against disease. People who have AIDS are vulnerable to serious illnesses which would not be a threat to anyone whose immune system was functioning normally. These illnesses are referred to as "opportunistic" infections or diseases.

What causes AIDS?

Investigators have discovered the virus that causes AIDS. Different groups of investigators have given different names to the virus, but they all appear to be the same virus. The virus is called human T-lymphotropic virus, type III (HTLV-III); lymphadenopathy associated virus (LAV); or AIDS related virus (ARV). Infection with this virus does not always lead to AIDS. Preliminary results of studies show that most infected persons remain in good health; others may develop illness varying in severity from mild to extremely serious.

What are its symptoms?

Most individuals infected with the AIDS virus have no symptoms and feel well. Some develop symptoms which may include tiredness, fever, loss of appetite and weight, diarrhea, night sweats, and swollen glands (lymph nodes)—usually in the neck, armpits, or groin. Anyone with these symptoms which continue for more than two weeks should see a doctor.

Who gets AIDS?

Ninety-four percent of the AIDS cases have occurred in the following groups of people:

- Sexually active homosexual and bisexual men with multiple partners, 73 percent;
- Present or past abusers of intravenous drugs, 17 percent;*
- Persons with hemophilia or other coagulation disorders, 1 percent;
- Heterosexual contacts of someone with AIDS or at risk for AIDS, 1 percent;
- Persons who have had transfusions with blood or blood products, 2 percent.

Some 6% of patients do not fall into any of these groups, but researchers believe that transmission occurred in similar ways. Infants and children who have developed AIDS may have been exposed to HTLV-III before or during birth, or shortly thereafter, or may have a history of transfusions. Some patients died before complete histories could be taken. Special studies of risk factors are under way with each of these groups considered to be at increased risk for getting AIDS.

What is the geographic distribution of reported AIDS cases?

Thirty-six percent of the cases in the U.S. are reported from New York State and about 23 percent from California. AIDS cases have been reported from 46 states, the District of Columbia, Puerto Rico, and more than 35 other countries.

How contagious is AIDS?

Casual contact with AIDS patients or persons who might be at risk for the illness does *not* place others at risk for getting the illness. No cases have been found where AIDS has been transmitted by casual household contact with AIDS patients or persons at higher risk for getting the illness. Although the AIDS virus has been found in saliva and tears, there have been no cases in which exposure to either was shown to result in transmission. Ambulance drivers, police, and firefighters who have assisted AIDS patients have not become ill. Nurses, doctors, and health care personnel have not developed AIDS from caring for AIDS patients.

However, health care and laboratory workers should follow safety procedures carefully when handling any blood and tissue samples from patients with potentially transmissible diseases, including AIDS.

How is AIDS transmitted?

AIDS is spread by sexual contact, needle sharing, or less commonly, through blood or its components. The risk of getting AIDS is increased by having multiple sexual partners, either homosexual or heterosexual, and sharing of needles among those using illicit drugs. The occurrence of the syndrome in hemophilia patients and persons receiving transfusions provides evidence for transmission through blood. It may be transmitted from infected mother to infant before, during, or shortly after birth.

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*In addition, a certain number of homosexual or bisexual men are also IV drug abusers.

How long after exposure to HTLV-III does a person develop AIDS?

The time between infection with the HTLV-III virus and the onset of symptoms (the incubation period) seems to range from about 6 months to 5 years and possibly longer. Not everyone exposed to the virus develops AIDS.

How is AIDS diagnosed?

There are no clear-cut symptoms that indicate the loss of immunity. The diagnosis of AIDS depends on the presence of opportunistic diseases. Certain tests which demonstrate damage to various parts of the immune system, such as specific types of white blood cells, support the diagnosis. The presence of opportunistic diseases plus a positive test for antibodies to HTLV-III can also make possible a diagnosis of AIDS.

Is there a laboratory test for AIDS?

As with most other infections, there is no single test for diagnosing AIDS. There is now a test for antibodies (substances produced in the blood to fight disease organisms) to the virus that causes AIDS. Presence of HTLV-III antibodies means that a person has been infected with the AIDS virus; it does not tell whether the person is still infected. The antibody test is used to screen donated blood and plasma and assist in preventing cases of AIDS resulting from blood transfusions or use of blood products, such as Factor VIII, needed by men with hemophilia. The test is also available through private physicians, most state or local health departments and at other sites.

What are some of the diseases affecting AIDS patients?

About 85 percent of the AIDS patients studied have had one or both of two rare diseases: *Pneumocystis carinii* pneumonia (PCP), a parasitic infection of the lungs; and a type of cancer known as Kaposi's sarcoma (KS). KS usually occurs anywhere on the surface of the skin or in the mouth. In early stages, it may look like a bruise or blue-violet or brownish spot. The spot or spots persist, and may grow larger. KS may spread to, or appear in, other organs of the body. PCP has symptoms similar to any other form of severe pneumonia, especially cough, fever, and difficulty in breathing. Other opportunistic infections include unusually severe infections with yeast, cytomegalovirus, herpesvirus, and parasites such as *Toxoplasma* or *Cryptosporidia*. Milder infections with these organisms do not suggest immune deficiency.

Is there a danger of contracting AIDS from donating Blood?

No. Blood banks and other blood collection centers use sterile equipment and disposable needles. The need for blood is always acute, and people who are not at increased risk for getting AIDS are urged to continue to donate blood as they have in the past.

How is AIDS treated?

Currently there are no antiviral drugs available anywhere that have been proven to cure AIDS, although the search for such a drug is being pursued vigorously. Some drugs have been found that inhibit the AIDS virus, but these do not lead to clinical improvement. Though no treatment has yet been successful in restoring the immune system of an AIDS patient, doctors have had some success in using drugs, radiation, and surgery to treat the various illnessess of AIDS patients. Therapeutic agents are needed for all stages of AIDS infections, to block action of the virus once infection has occurred, and to build up immunity in patients who have developed AIDS symptoms. Eventually, a combination chemotherapy to combat the virus and restore the immune system may be the most effective therapy. (*Pneumocystis carinii* pneumonia, for example, can be treated with antibiotics. Interferon, a virus-fighting protein produced naturally by the body, has been used with some success against Kaposi's sarcoma. Natural and recombinant interleukin preparations are being used in an attempt to repair the immunologic deficiencies in AIDS patients.)

Can AIDS be prevented?

Yes. Cases of AIDS related to medical use of blood or blood products are being prevented by use of HTLV-III antibody screening tests at blood donor sites and by members of high risk groups voluntarily not donating blood. Heat treatment of Factor VIII and other blood products helps prevent AIDS in patients with hemophilia and other clotting disorders. There is no vaccine for AIDS itself. However, there is good reason to believe that individuals can reduce their risk of contracting AIDS by following existing recommendations. Communities can help prevent AIDS by vigorous efforts to educate and inform their populations about the illness, with special emphasis on educational activities for members of high risk groups. Meanwhile, the discovery of the AIDS virus and methods developed for producing large quantities of the virus for experimental and other purposes enables scientists to work at developing a vaccine.

The Public Health Service recommends that the following steps be taken to prevent spread of AIDS:

- Do not have sexual contact with persons known or suspected of having AIDS.
- Do not have sex with multiple partners, or with persons who have had multiple partners.
- Persons who are at increased risk for having AIDS should not donate blood.
- Physicians should order blood transfusions for patients only when medically necessary. Health workers should use extreme care when handling or disposing of hypodermic needles.
- Don't abuse IV drugs. If you use IV drugs, then don't share needles or syringes (boiling does not guarantee sterility).
- Don't have sex with people who abuse IV drugs.
- Don't use inhalent nitrites (poppers). Their role as a cofactor for KS is being investigated.

Special recommendations for persons with positive HTLV-III antibody tests have been made to further prevent the spread of AIDS.

- A regular medical evaluation and follow-up is advised for persons with positive tests.

- Persons with positive blood tests may pass the disease on to others and should not donate blood, plasma, body organs, other tissue, or sperm. They should take precautions against exchanging body fluids during sexual activity.

- There is a risk of infecting others by sexual intercourse, sharing of needles, and possibly, exposure of others to saliva through oral-genital contact or intimate kissing. The effectiveness of condoms in preventing infection with HTLV-III is not proved, but their consistent use may reduce transmission, since exchange of body fluids is known to increase risk.

- Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.

- Women whose sexual partner is antibody-positive are themselves at increased risk of acquiring AIDS. If they become pregnant, their children are also at increased risk of acquiring AIDS.

Revised recommendations will be published as additional information becomes available. Further information about AIDS may be obtained from your local or state health department or your physician. The Public Health Service AIDS hotline number is 1-800 -447-AIDS. Atlanta area callers should dial (404) 329-1295.

Question: Considering the level of public concern, do you feel additional efforts should be made to inform and educate the public?

Answer: As noted in the previous answer, we are making substantial efforts to inform and educate the public. We have plans currently underway to expand this and implement a major national information/education campaign. The PHS agencies will work with the press so that the media can prepare accurate stories on AIDS. We will prepare releases about the transmission of AIDS and current research findings on all aspects of AIDS and other materials for the press, act as liaison with various groups carrying out public information and education programs on AIDS, and communicate with Congress, organizations, and the public through correspondence and briefing sessions.

We will continue to provide information about AIDS through MMWR articles, journal articles, bulletins, conferences, workshops, press briefings, talk shows and news shows, and the national AIDS hotline. The Fact Sheet About AIDS will be updated on a regular basis and distributed widely through all PHS agencies, to opinion leaders, interested groups, and all segments of the public. Videotapes will be made available with updated information on the HTLV-III antibody test and heterosexual transmission. Work will be done with outside groups to assist in sponsoring television and/or radio public service announcements regarding the AIDS hotline, information on transmission risks, the safety of the blood supply, the danger of IV drug use, and the fact that casual contact does not transmit AIDS.

In addition, we are planning to update and distribute selected information about AIDS to the following target populations: general public not specifically at risk, homosexual and bisexual men, adolescent youth who may become sexually active, hemophiliacs, IV drug abusers, female sexual partners of high risk individuals, and health-care workers.

Efforts are also being made through cooperative agreements with several States to demonstrate the impact of current health education and risk reduction methods, and to test innovative approaches to prevent the spread of AIDS. We are continuing to work with the United States Conference of Mayors to promote AIDS health education and risk reduction efforts of 19 community-based organizations.

Question: Can you describe for us how the Department is conducting the various studies and research programs for AIDS, and how resource allocation decisions are made?

Answer: The Department conducts AIDS studies and research programs through four PHS agencies - NIH, CDC, ADAMHA and FDA. Activities and studies are both intramural and extramural. Through their intramural programs, these agencies employ the Nation's best scientists and other medical personnel in a high priority effort to make maximum progress in our fight against AIDS. Additionally, through their extramural programs, these agencies enlist the efforts of the Nation's best research institutions and research scientists, the State and local health departments, the Nation's blood banks and many National organizations representing the groups most affected by AIDS.

The resources for AIDS grew from a level of $5.5 million in FY 1982 to $126.3 million in FY 1986. The PHS resource level grew each year as the Department identifies opportunities for expanding its efforts against this disease. The PHS, through its Executive Task Force on AIDS, monitors continually plans versus accomplishments and solicits the identification of new avenues for accelerated progress in controlling this disease. The Assistant Secretary for Health serves as Chairman of the Executive Task Force on AIDS, and therefore reviews and acts upon the major program and resource allocation decisions affecting AIDS. This monitoring process permits the PHS to explore and pursue every reasonable opportunity to bring this disease under control.

Question: What research objectives are being considered for expansion and what additional resources may be needed to allow for these efforts?

Answer: The Public Health Service is considering several research objectives for expansion in 1986, as well as some new research objectives.

- o Development of agents with activity against the AIDS retrovirus.
- o Further development of vaccines of viral origin.
- o Use of active antiviral agents for treatment of AIDS patients not included in clinical trials.
- o Accelerated development and testing of drugs for the treatment of AIDS and opportunistic infections.
- o Establishment of ten AIDS evaluation units to screen antivirals and conduct clinical studies. Efforts would be expanded for the development and evaluation of drugs for the treatment of opportunistic infections in AIDS patients.
- o Clarification of the epidemiology and natural history of HTLV-III infection.
- o Expansion of international efforts including: (a) Natural history studies in homosexual populations in the Caribbean, (b) Natural history studies of heterosexually transmitted AIDS in Zaire, and (c) Studies of vertical transmission from mother to newborn (common in Africa, others).
- o Expansion of Educational Assistance to States for Drug Abuse aspects of AIDS. This would include both in-service and in-training in the neuropsychiatric and drug abuse areas related to AIDS.
- o Expansion of the research base in mental health and drug abuse areas.

It is estimated that an additional $70 million above the FY 1986 request would be necessary to expand these objectives.

Question: Is the Department considering any new objectives and areas of investigation, education, and data gathering that this committee should know about?

Answer: There are several new and expanded objectives that the Public Health Service is considering for Fiscal Year 1986. The following represents a few of the major initiatives being considered.

- Expansion of the Development Therapeutics Program to acquire, screen, select, formulate, perform toxicological research, and synthesize large-scale bulk pharmaceuticals for new drugs and lead compounds to treat AIDS.
- Expansion of a program to develop vaccines of viral origin and to conduct confirmatory studies in higher primates.

- Expansion of studies to clarify the epidemiology and natural history of HTLV-III infection to include testing for HTLV-III antibody and viral isolation.
- Making drug therapy available to those AIDS patients that can not be enrolled in formal clinical trials. This would be done only after the efficacy of the drug is demonstrated.
- Establishment of ten new AIDS evaluation units in 1986 to screen for antivirals and conduct clinical studies.
- Expanded efforts for the development and evaluation of drugs for the treatment of opportunistic infections in AIDS patients.
- Initiation of epidemioligic studies to determine trends of HTLV-III exposure among drug users and prison inmates.
- Initiation of training and technical assistance efforts to assist health care providers to more effectively address the needs of drug users at high risk for developing AIDS. Technical assistance would be provided to mental health care providers and researchers on methods and procedures to care for AIDS patients.

QUESTIONS SUBMITTED BY SENATOR WILLIAM PROXMIRE

Question: Dr. Mason, as we intensify the use of the AIDS screening test, many apparently healthy Americans will be identified as carrying the AIDS antibody. Can these potential victims look forward to a time -- say five or ten years -- when they will no longer have to worry about contracting AIDS or is the incubation period completely unpredictable?

Answer: The time between infection with HTLV-III and the onset of symptoms (the incubation period) seems to range from about six months to five years and possibly longer. Preliminary studies in homosexual men infected with HTLV-III indicate that five to ten percent will develop AIDS within two to five years after becoming infected; others will remain asymptomatic or develop other HTLV-III infections.

Question: Dr. Mason, a Jack Anderson column appearing in yesterday's Washington Post referred to a patent war between France and the United States over an AIDS blood-testing kit. The article quoted the director of France's Pasteur Institute as saying: "There is a situation which can create a very difficult climate and will certainly not contribute to the conditions of an effective cooperation."

What's your response to that statement?

Answer: The Pasteur Institute claims regarding the invention of the AIDS blood test kit were first raised by representatives of the Institute at a meeting with staff from the Public Health Service in early August 1985. The Department concluded that the most oral representations made by the Institute at that meeting were not substantiated and that there is no basis for the French claim that the Department's patent is invalid or that they should be given a share of the royalties from the patent.

Since that time, we exchanged additional correspondence with the Pasteur Institute and invited them to submit more detailed written material in support of their claim. We have every desire to reach a resolution of this matter short of litigation and in a manner that will permit the continuation of the excellent scientific cooperation that exists between the two countries. A proposed process for resolving the matter amicably and expeditiously was communicated to the Pasteur Institute on October 16, 1985. We look forward to working with the French to resolve this issue as quickly as possible.

NATIONAL INSTITUTES OF HEALTH

Questions Submitted by the Subcommittee

Question: Is the biomedical research community fully mobilized for this expanding research effort for AIDS?

How would you describe the comparative level of effort being made by the intramural and extramural research programs?

How can we motivate more of our top research scientists to direct their attention to AIDS research?

Answer: The biomedical research community is well mobilized to respond to the expanded research effort on AIDS. The scientific and health issues that have emerged as a result of AIDS are of such a challenging and urgent nature that a significant segment of the biomedical research community is already working or planning to work in this area. With the additional funding requested, we expect more scientists from the closely related fields of virology, immunology, and infectious diseases to bring their expertise to bear upon the complex questions posed by AIDS. As this occurs, it is also anticipated that established scientists who are currently leaders in AIDS research will take a broader role by directing research teams, thereby expanding their sphere of influence while at the same time attracting and training less experienced scientists in AIDS research. These factors should be sufficient to provide the motivation necessary for more of our top scientists to continue to direct their attention to AIDS research.

There is an extensive amount of work being performed in both the intramural and extramural research programs. The intramural research effort has been complemented by a network of research grant and contract support and cooperative agreements which are closely integrated. Within the 1986 amended President's Budget, we estimate that approximately 70 percent of the AIDS funding will be devoted to extramural research efforts, while about 30 percent will support intramural activities. Through the intramural program we can mobilize resources and/or change directions in research to exploit new leads rapidly. If shown promising, even on a small scale, these leads can be pursued through a more comprehensive or major effort through the extramural program. Some projects, such as the clinical testing of antiviral agents on a large scale, must be undertaken extramurally in order to obtain the numbers of patients required as well as to establish geographically dispersed locations that will increase accessibility for patients who wish to participate in experimental protocols.

Transmission

Question: Is NIH sponsoring any studies which will provide more conclusive information on the routes of transmission, the degree of transmissibility, etc.?

Is AIDS transmitted differently and are the affected populations different between the United States and other countries such as the Central African countries and European countries?

-- Are you doing any studies which will provide information on the impact of the disease worldwide?

-- Will your studies provide any estimate of the possible impact of the disease worldwide, particularly in the developing countries?

Answer: The NIH continues to support an extensive series of studies designed to provide more information concerning routes of transmission and degree of transmissibility of HTLV-III. The data from these studies are obtained from both an epidemiological and a laboratory/clinical research perspective. Currently, the sexual and blood and blood product transmission routes are the only two defined modes of documented transmission. The National Institute of Allergy and Infectious Diseases (NIAID) is sponsoring five contracts to study the natural history of AIDS among over 5,000 homosexual men in Baltimore, Chicago, Los Angeles, Pittsburgh, and San Francisco. The National Cancer Institute (NCI) has studies in various populations including i.v. drug abusers, health care workers, etc. The NIAID is sponsoring studies of Haitian mothers and children at risk for AIDS and studies of AIDS among Haitians in Haiti. NIAID and NCI have studies in Central Africa and the NIAID and the CDC have a large collaborative effort in Zaire. Studies by NIAID and NCI are also under way in other African countries and the Caribbean. The National Heart, Lung, and Blood Institute (NHLBI) is supporting a major epidemiologic study of blood donors and recipients in Los Angeles, New York City, San Francisco, and Miami. In all these studies, a major focus is on routes of transmission and factors influencing the development of disease.

It appears that AIDS is transmitted the same ways in all parts of the world, namely through sexual contact or intravenous contact with contaminated blood or blood products. However, there appear to be differences in the affected populations. In the United

States, homosexual and bisexual men and intravenous drug users are the groups at highest risk. In Africa, the male to female ratio is closer to 1:1, which suggests that heterosexual spread is the predominant means of transmission. The spread of the disease in Europe appears similar to that in this country.

The studies described above will not immediately provide an estimate of the possible impact of the disease worldwide; however, collaborative efforts just beginning with other countries and the World Health Organization may provide more detailed information in the future. Moreover, findings that emerge from studies of the transmission of the disease through blood and blood products may have direct applicability anywhere in the world where blood and blood products are transfused. In addition, testing for antibodies to HTLV-III has shown that there are areas in equatorial Africa where substantial populations have detectable antibody, a situation which appears to have existed for possibly more than a decade. There also is the paradox which suggests that there are areas of antibody positivity which are not congruent with high attack rates of AIDS. A complicating feature is the recent discovery of an HTLV III-like virus found in indigenous African green monkeys (which do not get AIDS). This virus appears to be related to simian T cell lymphatropic virus (STLV), another member of the HTLV-III subgroup, which causes disease in rhesus monkeys. The antibodies to HTLV-III, STLV, and the African green monkey virus are cross-reactive to some degree. However, the status of the HTLV-III antibody found in Africa is not perfectly clear. It may be that the widely prevalent antibody is actually directed to HTLV-III-related monkey viruses. The sorting out of these possibilities relative to disease incidence could have profound world-wide implications.

Clinical Trials

Question: If you feel it is important to do controlled clinical trials, what can be done to provide access to these trials to larger numbers of individuals with AIDS?

-- Do you feel that there is a need to have more physicians and scientists involved in clinical studies around the country?

-- If so, is the lack of them now due to lack of interest? In doing the work?

-- Lack of drugs available for testing?

-- Lack of funding?

-- What funding would be required to make treatments available?

Answer: It is only very recently that the first drugs have shown any promise in treating AIDS. As the first drug, suramin, was found to have an antiviral effect _in vitro_, the NIH effort was expanded. Several additional drugs are just now showing promising early test results, although no therapeutic benefit is as yet claimed. These are now in limited human AIDS trials at NIH and elsewhere, as well as in an animal model. The identification of candidate drugs, with at least an effect in vitro against the virus, immediately suggests large clinical trials. Because such an effort would demand an integrated program, the NIAID and NCI have collaborated to develop a system for clinical investigation involving multiple steps and decision processes, ranging from drug discovery to phased clinical trials. Access to these trials by larger numbers of individuals with AIDS would be possible with the establishment of a significant number of AIDS Treatment Evaluation Units around the country with the expertise and support to perform clinical studies and widen the availability of clinical protocols in which AIDS patients could participate under carefully monitored conditions. We believe there are a number of experimental drugs available now that should be tested, and we will be screening for and attempting to develop new drugs to put into the "pipeline." The establishment of six to ten nationwide AIDS treatment evaluation units in the areas of greatest geographic incidence in FY 1986 would cost approximately $20 million. Additional new initiatives in therapeutic intervention are estimated at $14.7 million for FY 1986. A supplemental request for these amounts is under consideration at OMB. When added to the amounts available within the amended President's Budget, a total of $52.4 million would be devoted to the treatment of AIDS and the opportunistic infections in 1986.

In summary, we believe there are drugs for testing now, and that with the approach and resources described above, access to these trials can be provided to a larger number of individuals with AIDS.

Question: What research objectives are being considered for expansion at the NIH and what new initiatives may be taken in FY 1986?

In your opinion, what additional resources would be required to fund these expanded and/or new objectives?

Answer: Current research directions and objectives emphasize studies of the chemistry and biology of the causative virus; basic studies supporting the development of reliable diagnostic tests for AIDS; epidemiologic studies; work aimed at reconstituting the immune system in AIDS patients; inhibiting and eradicating the retrovirus (HTLV-III) with antiviral agents and controlling the opportunistic infections and cancers characteristic of the disease; application of several techniques to the development of vaccines, including the search for better animal models for AIDS; studies aimed at more effective screening of donated blood; and special emphasis on drug research and testing in the treatment of AIDS.

Rapid advances are being made in identifying antiviral compounds that have some anti-reverse transcriptase activity in the laboratory. Some of these may warrant more thorough study. Interesting findings in the laboratory leading to the development of new drugs and new therapeutic modalities, as well as leads on viral vaccine development, also merit further study. Consequently, the NIH has identified a number of new initiatives that could be pursued in 1986. Included among these are the following:

A. DEVELOPMENT AND TESTING OF DRUGS FOR THE TREATMENT OF AIDS AND OPPORTUNISTIC INFECTIONS

Major efforts are currently under way in the intramural clinical facilities of the NIAID and NCI to evaluate antiviral agents and immune reconstitution in AIDS and AIDS-related-complex patients. Investigators in the NIAID and the NCI are studying the use of suramin as an antiviral agent, and NCI investigators have a program to screen for new antivirals and evaluate other candidate antivirals developed by industry. In addition, NIAID investigators are studying a number of immunomodulators such as interleukin-2 and are attempting procedures such as bone marrow transplantation in an attempt to reconstitute the immune system. Studies are also under way to evaluate drugs for the treatment of the opportunistic infections to which most AIDS patients succumb.

In addition to these research efforts, the NIAID and the NCI have developed a collaborative plan for the development and testing of drugs for the treatment of the AIDS retrovirus as well as the concomitant opportunistic infections:

1. Acquisition

The NCI has already screened nearly 500,000 compounds for antitumor activity. All this information is available on a computerized database called the Drug Information System (DIS), which stores information on the preclinical data of new drugs, representing the largest database of its kind in the world. The system is interactive and allows the retrieval of this information in seconds.

Specifically, DIS includes chemical structure, inventory supplies, physical property information, and structure-activity analysis on nearly one-half million drugs. Thus, as new lead compounds are discovered by the screening effort, precise information (including available supplies) can be immediately accessed for testing. This system will be made available to the screening effort immediately without need for additional resources.

Already, DIS has proved a potentially invaluable acquisition database. Analogs related to nucleosides with anti-HTLV-III activity have been identified and placed into intramural screens. As predicted by structure-activity analysis, all have *in vitro* activity against the virus. Thus, there are lead compounds that could be immediately expedited into clinical trials.

Acquisition of other lead compounds will be expedited by the establishment of screening efforts in NIAID and National Cooperative Drug Discovery Groups by NCI. Recent advances in molecular biology, medicinal and organic chemistry, pharmacology and biochemistry provide unprecedented opportunities for the design of powerful antiviral therapies with unique modes of action. The complexities of these modern approaches and the urgency of the AIDS problem demand that the talents of the most creative and dedicated scientists be enlisted in concert. To accomplish this, the NCI proposes to establish a national support mechanism to permit the most outstanding scientists in viral biology, chemistry, pharmacology, and biochemistry to interact. Because few, if any, institutions possess a critical mass of all the varied talents required, National Cooperative Drug Discovery Groups for anti-HTLV-III drugs will be implemented under the Cooperative Agreement mechanism. Each group will be multi-institutional and composed of outstanding investigators from academic, nonprofit research institutions and/or industry. The NCI and NIAID will participate as members of each group, but the groups will function under the leadership of group directors from outside the Government. This interaction of academic and nonprofit research institutions with industry and Government will expedite the efficient invention of new entities and strategies for AIDS treatment as well as their subsequent development to clinical trial and marketing.

2. Screening

The drug discovery phase of a new drug project is composed of two stages: new lead discovery and new lead development. Screening for new leads with anti-HTLV-III activity will be conducted by NIAID, predominantly utilizing the extramural contract system.

Lead improvement on a smaller scale will be carried out intramurally by the NCI, where staff have developed a permissive T-cell clone that is uniquely sensitive to the cytopathic effects of HTLV-III. This limited scale testing system has already identified two agents that appear capable of inhibiting viral outgrowth in AIDS patients: suramin and azidothymidine. The additional resources required by NCI will permit the continued specific lead development in the intramural program and pilot intramural clinical trials.

3. Drug Selection

The NIAID-NCI collaboration will cross administrative lines to ensure: (1) rapid analysis of all new data; (2) prompt decisions regarding selection of the most promising new compounds; and (3) follow-up on the progress of those functions that must be completed prior to INDA filing with the FDA. This operational process will parallel the Decision Network that has been established within the NCI, but will include representatives from both NIAID and NCI.

The AIDS Drug Selection Committee will evaluate screening data to prioritize those new drugs that should be expedited to formulation and production, toxicology, and clinical trials.

4. Formulation and Production

The NCI currently has several groups of contracts in force to formulate and produce new anticancer drugs; these will be expanded to include anti HTLV-III drugs:

Off-site Quick Reaction Synthesis
Resynthesis
Preparation of Bulk Chemicals and Drugs
Production and Development of Pharmaceutical Drug Forms
Development of Dosage Forms and Delivery Systems
Storage and Distribution of Clinical Drugs

These contracts will be supplemented as necessary to provide drugs for NCI toxicology and intramural trials as well as large-scale NIAID clinical programs.

5. Toxicology

The NCI supports contracts for preclinical toxicology of new anticancer drugs. These research contracts provide toxicity data and determine end organ toxicities in these systems. These data are important in determining not only safe starting doses for clinical trials but also provide an early indication of the likely toxic endpoints for patients on study. Equally important, these research contracts are capable of sophisticated preclinical pharmacology and bioavailability studies. This information is critical in determining whether achievable drug blood levels in vivo are capable of in vitro viral inhibition, whether oral formulations of a drug provide adequate bioavailability, and whether a given agent is capable of penetrating the blood-brain barrier. This latter determination is critical in view of the ability of HTLV-III to replicate in the brains of AIDS victims.

Again, these contracts would be supplemented to meet the requirements of the NIAID-NCI collaborations.

6. Clinical Studies

This program is for human testing of candidate AIDS antiviral drugs, immune enhancement agents, and procedures and agents for treatment of opportunistic infections and tumors. An RFP will be developed for the establishment of 6-10 AIDS treatment evaluation units in 1986, which will be operated analogous to existing NIAID vaccine evaluation units that have proven so successful.

B. NATURAL HISTORY OF AIDS IN HOMOSEXUAL MEN

The NIAID is currently supporting five extramural contracts in which cohorts of homosexual men in five cities (San Francisco, Los Angeles, Chicago, Pittsburgh, and Baltimore) are being followed closely to delineate the natural history of AIDS. In addition, a contract with the New York Blood Center and Memorial Sloan-Kettering Institute is following men in New York City who participated in past hepatitis B vaccine trials or are undergoing plasmapheresis for hepatitis B antigen. These natural history studies were awarded for a 5-year period before HTLV-III was established as the causative agent of the disease. These studies must now be supplemented to include testing for HTLV-III antibody and viral isolation.

In addition to the natural history and epidemiology studies in this country, most of the NIAID international efforts in AIDS research are also within this category. The NIAID is currently supporting, in collaboration with the CDC, a project to study AIDS in Zaire. In addition, studies are beginning in prostitutes in Kenya; these studies have direct relevance to similar studies in this country.

The NIAID proposes several important studies in addition to those currently under way in Zaire and Kenya: (1) natural history studies in homosexual populations in the Caribbean (Trinidad, Barbados, Surinam, Bahamas) and in Asia (Thailand and Singapore); (2) natural history studies of heterosexually transmitted AIDS in Zaire; (3) prospective studies of AIDS in female prostitutes in Kenya, Trinidad, Jamaica, Surinam, Zambia, and Thailand; (4) studies of vertical transmission from mother to newborn, which is common in Africa; (5) studies on cofactors such as parasitic infections and their role in the development of the disease; (6) the identification of nonhuman primate reservoirs in Africa; and (7) studies of racial/genetic factors that may influence acquisition of infection and expressions of disease; e.g., there is an unexplained difference in the rate of disease in those of African versus Asian descent in Trinidad.

C. AIDS VACCINE DEVELOPMENT AND TESTING INCLUDING DEVELOPMENT OF ANIMAL MODELS FOR AIDS

The NCI is pursuing the development of an HTLV-III vaccine using techniques to break up the whole virus and dissect those antigens that may prove useful as immunizing agents. Preparations using this approach are now in the stage of animal testing. The NIAID, as well as the NCI, is also pursuing the development of vaccines using recombinant DNA and monoclonal antibody technology. Some candidate vaccine preparations are currently being tested in animals and if efficacious, it is possible that human testing will be available within the next 1 to 2 years. The NCI has developed an RFA for grants to develop retroviral vaccines. The NIAID has been invited to co-sponsor this RFA. If vaccines become available for testing, three vaccine evaluation units (those appropriate for AIDS vaccine studies, i.e., University of Maryland, Baylor University, and University of Rochester) will be supplemented for phase I studies. Expansion of intramural research studies related to AIDS vaccine development utilizing recombinant DNA technology is proposed.

It is extremely important that an animal model be developed for AIDS that can be used in the evaluation of treatment modalities and vaccines prior to testing in humans. Although the chimpanzee appears to be a useful model, it is extremely expensive and in very limited supply. A major effort should be mounted to develop a less expensive and more practical animal model. Such efforts are under way at the NCI and also within the NIAID intramural research program.

D. AIDS OUTREACH ACTIVITIES

Advances in AIDS research must, of course, be transmitted to the public. The NIAID supports an AIDS outreach program that has held a series of conferences throughout the United States aimed primarily at health care professionals and public service personnel. These conferences have been very successful and in all cases have been oversubscribed.

The NIAID proposes the continuation of these types of outreach activities and the development of new ones. For example, packaged workshops on AIDS should be developed and made available for presentation at local and national professional and lay meetings. A recent workshop on AIDS presented by NIAID staff members and grantees was part of the program for the national meeting of the National Medical Association, and it was very well attended. Specialized conferences and workshops designed to bring the latest information on the treatment of AIDS patients will be presented in major metropolitan areas where there are large numbers of AIDS cases. These will be designed for physicians who are caring for the patients. These and other programs, perhaps through cooperation with organizations such as the Hospital Satellite Network, could be televised for distribution and viewing around the country.

Additional Resources

The recently completed PHS review of AIDS requirements identified $50.0 million in expanded and/or new initiatives in FY 1986. A supplemental request for this amount is under consideration at OMB.

Question: The AIDS research budget for NIH has increased from $44.1 million in 1984 to an estimated $63 million in 1985 and may reach $100 million or more in FY 1986.

-- Have the various institutes been able to increase the number of employees working on AIDS research (FTEs), given the increased research effort, without diminishing the work on other programs?

-- In your professional opinion, how many additional FTEs should be added to the NIH complement to allow the institutes to take maximum advantage of the additional resources?

  -- Do you have sufficient manpower to meet FDA requirements for monitoring clinical trials?

Answer: Through reassignment of staff, the NIH has a total of 192 FTEs involved in AIDS research in 1985. Personnel resources are monitored closely, with every effort made to minimize the impact on other programs. The amended President's Budget requested an increase of 52 FTEs for AIDS research in 1986, which would bring the total to 244 FTEs.

An expansion of the NIH research effort on AIDS would require an additional 70 FTEs over the amended President's Budget. Of this total, 14 additional FTEs would be required to meet FDA requirements for monitoring clinical trials.

Treatment Method

Question: In your professional judgment, what is needed and at what cost, to speed up the development and testing of new treatment methods for AIDS?

Answer: In order to speed up the development and testing of new treatment methods for AIDS, continuing efforts should be made to screen and discover new drugs with potential and to increase the numbers of institutions performing clinical studies with these drugs. A stock of antiviral drugs exists to which HTLV-III may be susceptible. One additionally has to consider that retroviruses have special features in their life cycle which could make them quiescent in the DNA of the cell for indeterminate time intervals, during which they would not be susceptible to any drug which acts by negatively affecting the life cycle of the virus. However, many potential agents have been developed for other viruses that can be readily tested in AIDS. A number of these, such as Ribavirin and Foscarnet, are being brought into trials under Investigational New Drug (IND) applications. A much richer source of analogous compounds, generally in the family of substituted purine and pyrimidine analogs, exists in the computerized drug index compiled for antitumor agents. Recently, NIH scientists have used this index to search for activity of drugs in vitro against HTLV-III. In developing antiviral agents, drug companies have variants of current drugs as well as research data. These leads should be exploited. As likely drugs become available, an NIAID/NCI Drug Selection Committee will serve to define the drugs with which to initiate a treatment protocol, and whether to remove or supplant a drug currently in a trial, if a new drug appears more effective.

Approximately $12.0 million is available within the amended President's Budget for research on the treatment of AIDS and $5.7 million is available for research on treatment of the opportunistic infections. In our professional judgment, an additional $33.7 million and $1.0 million, respectively, could be wisely expended in the expeditious development of new treatment methods for AIDS and the opportunistic infections. A supplemental request for these amounts is under consideration at OMB.

Question: How are resource allocation and research policy and direction decisions made at the NIH with respect to AIDS?

Have you, or do you plan to identify, a coordinating group or task force to assist in making these decisions?

Have you chosen a leader for this group?

Answer: In 1982 an NIH Working Group on AIDS was established to coordinate and exchange information among the Bureaus, Institutes, and Divisions of NIH as well as the Centers for Disease Control (CDC) and the Food and Drug Administration (FDA). This working group was replaced by the NIH AIDS Executive Committee, which was established in June 1984. In order for the NIH to develop an even broader capacity for coordination and planning of AIDS research, in the past week I have designated Dr. Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases, as the NIH AIDS Coordinator. Dr. Fauci will accompany and/or represent me at PHS Executive Task Force meetings, will co-chair with me the NIH AIDS Executive Committee, and will assist me in providing guidance and direction for NIH-wide scientific, policy, and resource allocation decision making. I have also asked Dr. Fauci to reconstitute the NIH AIDS Executive Committee. One of the first tasks of the newly revised NIH AIDS Executive Committee will be to develop an NIH coordination plan that ensures an internal framework adequate to keep pace with an increasing number of issues, to address emerging areas of concern and new issues, identify gaps and redundancies, to supply senior officials with timely and consistent information and data, and to provide for appropriate development and review of all official documents.

At the Bureau, Institute, and Division level, overall resource allocations are made by the institute directors with input from institute executive committees, working groups and program directors, augmented by the advice of advisory committees, boards, and councils that utilize all available national and international expertise.

Animal Model

Question: I understand that the NIH is planning on using chimpanzees as an animal model.

- Are chimpanzees susceptible to the AIDS virus or AIDS-related viruses?
- What are the plans to use rhesus monkeys in this endeavor--I understand that they are susceptible to AIDS-related viruses.

Answer: Chimpanzees are susceptible to the AIDS (HTLV-III) virus and are presently being used as an animal model in studies of virus transmission and other related research. However, chimpanzees that have been infected with the AIDS virus for as long as 2 years have not experienced a fatal clinical disease similar to

AIDS patients. Chimpanzees do experience measurable changes in their immune and lymphatic system following infection, and the virus does replicate in the chimpanzee; but overt clinical signs associated with infection are not apparent.

So far, other primates tested are infected only sporadically, and both regular virus isolation and antibody responses are more tenuous. No signs of disease have been observed in lower primates. Antibody responses could be elicited in lower primates by either infectious virus or by vaccine preparations. The characterization of HTLV-III infection (AIDS-related virus) in rhesus monkeys may provide a model for HTLV-III infections in man. This virus-host system is currently under investigation. Rhesus monkeys are susceptible to several retroviruses that cause fatal AIDS-like illnesses in these and several other macaque species. One of these viruses is a Type D retrovirus that causes simian acquired immunodeficiency disease (SAIDS). It is not as closely related to the human AIDS virus as a more recently identified virus, STLV-III (for simian T cell lymphatropic virus), that was associated with the deaths of a number of animals at the New England Regional Primate Center. STLV-III is closely related to HTLV-III and distinguishable only by sensitive methods of molecular genetic characterization. Because they cause a reproducible clinical syndrome like AIDS, these viruses offer very promising models for studies of vaccine development and therapy. Although illness has not been produced with HTLV-III in rhesus monkeys to date, it may be possible to perform some vaccine development experiments in these animals.

Question: We have been told that NIH has several projects around the country to study individuals at risk to AIDS.

-- What is being learned from these studies?

We have heard that you are planning to cut back on three studies and are planning to terminate them earlier than originally planned.

-- Is this information correct?

-- Was this decision based on scientific judgment or financial judgment?

-- How much would it cost to complete these studies as planned?

Answer: The NHLBI is supporting several research projects around the country dealing with the transmission of AIDS by blood and blood products. One such study has shown that among 13 cases of transfusion-associated AIDS, four had received blood from a donor who later developed the syndrome, three are still under investigation, and a healthy carrier has been identified in six cases. Another study is attempting to determine the extent of immunologic changes in patients with hemophilia who routinely receive clotting factor concentrates. The NHLBI is also supporting a major multicenter study of immunologic alterations that occur following multiple blood transfusions in various groups and the possible association of these changes with the development of AIDS. The NHLBI also supports an evaluation of blood donors for antibody to HTLV-III in high prevalence areas. From early September 1984 through early February 1985 serum samples were collected from over 201,000 blood donors in Los Angeles, New York City, San Francisco, and Miami. These samples were taken before HTLV-III antibody testing was available. The sera are now being tested and the donors whose serum samples show the presence of antibody to HTLV-III will be asked to participate in a study to follow their immunologic and virologic status over a 3-year period. Similarly, the recipients of blood from the HTLV-III antibody donors will also be identified, enrolled in the study and followed prospectively. The consequences of exposure to HTLV-III antibody-positive blood should be elucidated by the end of the study.

The NIAID is currently supporting five extramural contracts in which cohorts of homosexual men in five cities (San Francisco, Los Angeles, Chicago, Pittsburgh, and Baltimore) are being followed closely to delineate the natural history of AIDS. In addition, a contract with the New York Blood Center (NYBC) and Memorial Sloan-Kettering Institute is following men in New York City who participated in past hepatitis B vaccine trials or are undergoing plasmapheresis for hepatitis B antigen. For comparison, a group of homosexual men in a low risk area (Ithaca, New York) are also included in this study. These studies will provide valuable information regarding the transmissibility of the disease and on possible co-factors involved in the development of full-blown AIDS. Important information such as the significance of HTLV-III antibody positivity as a predictor of who will get disease will only come from studies such as these. This type of information has important ramifications for future considerations by insurance actuaries, the military, etc.

Because of the size of these cohort studies, information unlikely to be obtained easily from any other investigations is becoming available. Data from four centers are being analyzed collectively and show that volunteers are rather similar in their social background and sexual experiences. They vary in the proportion who were positive for HTLV-III/LAV antibody by ELISA in 1984, from 23 percent in Pittsburgh to 55 percent in Los Angeles. Over 40 cases of AIDS have developed in participants who were at later stages of infection when they enrolled, but they are not being compared with those free of illness to search for prognostic clues. Although several other studies have shown that receptive anal intercourse confers the major risk of infection on homosexual men, preliminary analysis of data from the cohort studies suggest that certain practices (e.g., douche before intercourse) may promote infection further, while others (e.g., receptive oral-genital intercourse) do not. Another unique consequence of the scale of these studies is that with about 5 percent of the ELISA antibody-negative men seroconverting in the first 6 months of the study, some 150 such men are already available for more intensive investigation. Moreover, the work will permit examination of changes in this measure of immunity in either direction. The most important contributions of these studies are yet to come. Large numbers of infected individuals followed for a long period of time are necessary to determine the incidence of very infrequent complications of the infection (e.g., neoplasms).

These natural history studies were awarded for a 5-year period with an estimated budget figure before HTLV-III was established as the causative agent of the disease. It is now essential that these studies include testing for HTLV-III antibody and viral isolation. The costs for viral isolations are extraordinary. For example, a contract to perform 20 isolations per week in support of our intramural research costs approximately $500,000 per year. The contractors were given a supplement of approximately $2.5 million (to be shared by all of them) for viral isolation. This amount is not adequate for viral isolations over the life of the contracts; and it is of no help with the other expenses. Furthermore, concerns about confidentiality of the results have made it much more difficult to recruit study participants and have added to recruitment costs of the contracts. This has required all of them either to reduce their efforts or plan to terminate their contracts before the original expiration date. In my professional judgment, an estimated additional $4,750,000 in FY 1986 is needed to support the NYBC contract and natural history contracts through their originally scheduled time period. A supplemental request for this amount is under consideration at OMB.

Blood Test

Question: How good is the blood screening test and how much effort is being made to improve it?

In your opinion, should this effort be increased and if so, by how much?

Answer: The commercial assays that are currently available for screening blood donors are quantitative tests for HTLV-III antibodies. These tests have proven to be quite sensitive. New tests are under development that detect other HTLV-III antibodies. These second-generation assays should lead to the development of even more sensitive tests.

In addition, there is also a need to develop an assay to detect the presence of the virus itself. Some blood or bone marrow samples may be negative for antibodies to HTLV-III even though they may contain the virus. Therefore, methods to detect viral particles in clinical specimens as well as methods to reveal the HTLV-III genome integrated into cellular DNA would be extremely useful in detecting the virus in individuals who do not exhibit antibody to the virus. Approximately $1.2 million is available for NIH within the 1986 amended President's Budget for the development and evaluation of blood tests for AIDS.

Question: What is involved in vaccine development and why is it so expensive?

In your professional judgment, would additional funds speed up the development of an effective vaccine?

Answer: Vaccine development is a complex and lengthy process. The retrovirus causing AIDS has no known immediate animal-virus relatives which could be used as learning models. Retroviruses have special features which would tend to obviate some basic effective vaccine approaches, such as the use of inactive virus and nonpathogenic variants. Five additional paths of vaccine development can be considered which could be both safe and effective. Each of these could have several subset approaches. For example, antigens produced by genetic engineering may have to be expressed in bacteria, yeast, or mammalian cells. It is currently unknown which of them, if any, will be functionally useful.

Besides the number of possible approaches, two other problem areas can be defined. The HTLV-III virus isolates tend to vary significantly in some viral genes, which predicts that either a number of types exist, or that the viral antigenicity may readily change. In either case, the vaccine inoculum may have to be complex. Second, the only currently available animal model in which infection resembles the human disease after HTLV-III inoculation is the chimpanzee. Because of the scarcity of this species, "primate" vaccines will have to be developed in lower primates which are less adequate for protection studies in vivo.

The conventional steps in vaccine development are as follows:

1. Understanding the disease and the host

    a. Clinical recognition
    b. Specific diagnosis
    c. Natural history
    d. Epidemiology
    e. Pathogenesis
    f. Resistance modifiers
    g. Nature and duration of immunity

2. Understanding the pathogen

    a. Specific identification and characterization
    b. Cultivation
    c. Antigenic analysis
    d. Genetic determinants
    e. Infection of other species; animal models
    f. Properties

        (1) Determinants of infectivity
        (2) Determinants of virulence
        (3) Determinants of antigenicity
        (4) Determinants of immunogenicity

3. Construction of an inactivated vaccine

    a. Optimum growth of pathogen
    b. Identification of essential immunogen
    c. Purification of essential immunogen
    d. Production of antigen using recombinant DNA technology
    e. Artificial synthesis of antigen
    f. Selection of adjuvants, if necessary
    g. Demonstration of antigenicity
    h. Production of pilot lots

4. Construction of a live, attenuated vaccine

    a. Growth in acceptable cells, tissues or other cultures
    b. Satisfactory infectivity and antigenicity
    c. Demonstration of lack of virulence
    d. Demonstration of genetic stability (lack of reversion)
    e. Production of pilot lots

5. Testing of vaccines

    a. Inactivated

        (1) Early Phase 1 trials in humans
        (2) Challenge of immunized volunteers
        (3) Expanded trials to test antigenicity and transmissibility in semi-closed populations
        (4) Final test of safety and efficacy in open field trials in populations at high risk

    b. Live, attenuated

        (1) Early trials in humans, isolated, if necessary Step-wise Phase 1 trials of attenuated vaccine from adults with antibody to children without antibody
        (2) Challenge of immunized volunteers
        (3) Expanded trials to test antigenicity and transmissibility in semi-closed populations
        (4) Efficacy trials

            (a) By direct challenge of volunteers
            (b) By natural challenge of open populations

6. Production of commercial lots
7. Licensure
8. Professional and public acceptance

Progress in the development of a vaccine for AIDS is at Steps 3 and 4. Development of an effective vaccine will be particularly difficult, because the HTLV-III/LAV virus is an unconventional virus. Because of the very long incubation period of this disease, the target populations selected for immunization as a test of vaccine efficacy would have to be followed for many months or years to determine outcome. This will greatly increase the expense of a controlled trial, adding to the considerable expense already associated with the complex laboratory procedures--costly in terms of both materials and personnel--required to reach Steps 3 and 4 and to prepare candidate vaccines for Step 5.

In my professional judgment, additional funds would speed up the development of an effective vaccine although one cannot be certain that the approaches being taken will be successful. Additional funds would allow more approaches and more research groups to be involved. A supplemental request of $2,750,000 for 1986 is under consideration at OMB for studies in this area.

Question: If additional resources are provided by the Committee, will they enable the NIH to implement several new AIDS initiatives, particularly collaborative activity between institutes to develop and test drugs for the treatment of AIDS?

Answer: The NCI and the NIAID will develop and carry out a collaborative plan for the development and testing of drugs for the treatment of the AIDS virus as well as the opportunistic infections. This program could include screening for new antiviral drugs; the selection of drugs for clinical trials; preclinical toxicology, formulation, and pharmacology; investigational new drug preparation; and clinical studies of candidate antiviral drugs, immune enhancement agents, and procedures and agents for treatment of opportunistic infections and tumors.

Other new initiatives which could be supported include: expanded basic research; the development of candidate vaccines and their clinical evaluation; epidemiology studies on an international scale, with particular focus on those areas evidencing heterosexual transmission of AIDS; increased efforts in the development of an animal model; expansion of on-going studies in five U.S. cities on the natural history of AIDS; and enhanced outreach activities to provide information to health care providers and the general public as well as clinical investigators.

Question: HTLV-III has been isolated from some individuals who are negative for antibody to the virus as determined by commercial antibody assays. How can this problem of false-negative results with the antibody assay be resolved.

Answer: First of all very few people who are in high risk groups and thus may be suspected of carrying the virus fall into this category -- it is on the order of 1 percent of those who might be infected. Nevertheless, it does represent a real risk to the safety of the blood supply. NHLBI supports research in this area and will continue to solicit studies for development of reliable tests for the virus. A test for virus antigen used in combination with the antibody assay would detect virus-positive/antibody-negative individuals. Current methods for detection of virus in blood are laborious and expensive. Even expert laboratories can, at best, perform only 30 viral isolations per week. The Institute is supporting the development of rapid methods that can detect virus in infected blood cells of antibody-negative/virus-positive individuals. Some of the research approaches include a test for viral enzyme in the serum; assays to detect viral nucleic acid integrated into cellular DNA; and use of specific monoclonal antibodies to some of the viral proteins.

Question: The blood derivates used to treat hemophiliacs are heat-treated to inactivate potential viral contaminants such as HTLV-III. What are the NIH's plans regarding the inactivation of HTLV-III in blood components required for other genetic diseases?

Answer: The NIH hopes to solicit research on methods to inactivate or remove the virus in blood components, including complex protein mixtures and perhaps blood cells. Current procedures which include heat inactivation may effectively destroy the virus in blood derivatives (factor VIII concentrates, factor IX preparation, immune globulins). However, a number of blood fractions which cannot be prepared in a dry state, such as cryoprecipitate (source of factor VIII and a number of other large plasma proteins, including fibrinogen, von Willebrand factor and fibronectin) cannot survive heat treatment. Thus, other methods must be found to remove or inactivate the virus.

An even more difficult task may be to develop methods to inactivate the virus and the integrated viral genome in cellular materials, including blood cells and bone marrow, to assure recipient safety. In cellular material, especially lymphocytes, the viral genome may be integrated into host DNA and be unexpressed at time of blood or tissue donation. Methods to remove or inactivate such material may become particularly important to establish or retain the efficacy of various organ transplantation systems.

Question: Is the NIH doing anything to prevent AIDS in people at high risk for the disease, such as people who work in blood banks?

Answer: The NIH will award a contract before the end of the month to find antibodies and prepare an immune globulin to block and neutralize the AIDS virus in people who are at risk of being exposed to the virus. Once it is established that neutralizing antibodies to HTLV-III can be obtained in sufficient quantities, an immune globulin preparation will be formulated for either intramuscular or intravenous use. It will be manufactured in segregated equipment in accordance with FDA requirements, observing all quality control procedures. Once stability, potency and safety tests are satisfactorily conducted, the product will be clinically evaluated in groups of individuals having special exposures or susceptibilities to HTLV-III. Some specific opportunities for evaluation include post-transfusion prophylaxis for recipients belatedly discovered to have received blood products from an HTLV-III carrier; post-needlestick prophylaxis in health care workers; sexual partners of infected persons; and neonates from mothers who have HTLV-III markers.

Question: The licensed tests used in the blood banks to detect antibody to HTLV-III seem to yield false-positive results. Is the NIH doing anything to resolve this problem?

Answer: It is obvious that the current ELISA technology to detect antibody to HTLV-III is, at best, an interim measure. The current assay for HTLV-III antibodies utilizes disrupted, inactivated virus that contains many cell-associated components from the cell cultures in which the virus was grown. Antibodies to these cell components, and not to the virus itself, might contribute to the false-positive results that you refer to. The NIH (NHLBI) currently supports research to develop specific viral components by recombinant DNA techniques. This approach should yield highly purified viral components that are devoid of cellular contaminants. Viral recombinant products would replace the disrupted, inactivated HTLV-III that is currently used in the licensed assays. These new, second-generation assays should be more sensitive, specific and yield far fewer false-positive reactions.

QUESTIONS SUBMITTED BY SENATOR WILLIAM PROXMIRE

AIDS Vaccine

Question: Dr. Wyngaarden, on page 4 of your prepared statement you refer to the work the institutes are supporting on antigens that would produce antibodies to neutralize or protect against AIDS. If you produced a vaccine that produced protective antibodies, would the presence of those antibodies make it difficult to use a blood screening test to detect those exposed to the AIDS virus? In other words, would a vaccine recipient be apt to show up as a positive in a blood screening test?

Answer: At the present time insufficient information is available to answer this question. A number of likely vaccine preparations are being and will be considered against HTLV-III. The major antigenic determinants of interest are found in the external glycoprotein (gp120). It is clear from recent data, only some of which are published, that essentially all AIDS patients do have antibodies to gp120/gp160. Currently, the major reactive antibody in AIDS is directed against the viral gp41. Because ELISA or Western blot tests use whole virus, it is expected that vaccines could react positively. However, the most probable vaccine preparations will contain only gp120 determinants or both gp120 and gp41, whether these are natural or synthesized products. Since people infected with HTLV-III generally make a spectrum of antibodies to other viral proteins as well, which would not be a part of an HTLV-III vaccine preparation, the more complex antibody profile should differentiate between the vaccinated and the naturally infected individual.

Other avenues to be explored include development of blood tests for the virus itself, both in the plasma and in blood cells, for the viral genome, and especially for virus when antibody is already present. Some of the research approaches include a test for viral enzyme in the serum; assays to detect viral nucleic acid integrated into cellular DNA; and use of specific monoclonal antibodies to some of the viral proteins.

Sensitive Screening Test

Question: Dr. Wyngaarden, Dr. Katz's testimony on behalf of the Red Cross calls for "an even more sensitive screening test . . .for whole blood and its components." Dr. Katz adds that such a test should be able to detect intracellular virus so that transmission by leukocytes can be prevented for individuals who may not have free virus in the serum.

Can you tell us what steps the institutes are taking to develop such a test and how much it would cost to proceed with a full scale effort in fiscal year 1986?

Answer: NIAID scientists and others are preparing or have prepared antibodies in mice and rabbits to various components of HTLV-III. Toward this end they have entered into collaborations with outside investigators to produce AIDS virus polypeptides in E. coli and in baculovirus vector systems. The proteins generated from these sources will be used to raise antibodies in appropriate animals for use in an antigen detection system. NIAID investigators are trying to exploit a unique system involving human lymphocytes which continually produce large amounts of all viral proteins yet generate no infectious virus. Animals are being inoculated at the Frederick Cancer Research Facility with these viral-protein synthesizing cells as well as with purified AIDS viral polypeptides from this source to elicit a full spectrum of antibodies directed to the virus.

Although the development of an antigen detection system should theoretically be a more sensitive assay for the HLTV-III, NIAID and others, using hybridization in situ to monitor lymphocytes in patients from which virus can be isolated, have shown that only one cell in 50,000 to one cell in 500,000 contains viral RNA. This very low level of positive cells in patients who are antibody positive presents difficulties and will require time for the development of a sensitive antigen detection assay.

The National Heart, Lung, and Blood Institute currently supports a small research grant program for development of blood tests for AIDS. Some of the research in this program is directly applicable to the problem of detecting the virus. The Institute hopes to expand this program through new solicitations to develop sensitive tests for free virus, for cellular virus, and for integrated viral genome. Such tests would be helpful not only for reducing the small number of false negative individuals who are now donating blood but are not being identified by the current ELISA tests for antibodies, but would also be helpful in assuring that donated organs and tissues, including bone marrow, are free of AIDS virus infection.

Approximately $1.2 million is available for NIH within the amended President's Budget for development and evaluation of blood tests.

CENTERS FOR DISEASE CONTROL

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

Question. Would you briefly describe how CDC formulates its budget request for AIDS?

Answer. AIDS is a rapidly changing public health problem. There are still many unknowns and each time a new discovery is made, new issues and urgent needs are identified. The Acting Director, CDC, and other top CDC scientists with expertise in AIDS and senior managers meet weekly to review findings and events to date and develop plans for future activities. The most recent plans were based on CDC's best professional judgment of what needs to be accomplished, taking the following factors into account:

1) As AIDS reporting has increased, the number of requests to CDC for assistance in conducting surveillance and other AIDS activities have increased.

2) There has been a continuing need for epidemiologic studies to identify risks of disease transmission by studying behaviors and characteristics of infected populations, environmental factors, and other relevant factors.

3) Laboratory investigations continue to be needed to study the AIDS virus susceptibility to environmental agents, methods of isolation, presence in body fluids, testing procedures, and changes in its genetic makeup.

4) Since no vaccine or effective therapy is presently available, there is an urgent need for a prevention strategy based on screening the blood supply,

disseminating prevention guidelines, and encouraging behavior changes that reduce the risk of transmission among those at risk.

Question. For the last two years, we have received revised budget requests for AIDS which reflect an increase over the original budget submission for that year. Why is it so difficult to predict how much you will need for AIDS for the coming year, necessitating several revised budget requests throughout the year?

Answer. AIDS is a rapidly changing public health problem. Despite recent advances in our knowledge of AIDS, the number of AIDS cases and deaths and the number of individuals infected with the virus continue to grow at a rapid pace. There are still many unknowns, and each time a new discovery is made new issues and urgent needs are identified. For example, discovery of the AIDS virus in 1984 significantly increased the opportunities and funding for additional research. In addition, the release of the antibody test for use in screening the blood supply raised the issue of how to prevent risk group members from donating blood primarily to determine their HTLV-III antibody status.

The intense public attention and many unanswered questions about AIDS, as well as the seriousness of the condition, raise issues faster than they can be resolved. Consequently, it has been extremely difficult to predict changing agency needs during the year.

Question. The Administration's request for FY 1986 did not include funding for alternative blood testing sites, which separate potential AIDS-contaminated blood from the normal blood supply. You had requested funding for this in FY 1985. Why are you not requesting to continue this blood screening process in FY 1986?

Answer. CDC awarded funds in April with the clear purpose of underwriting the initial development of alternative sites and a laboratory capability for their support. All grantees understood that continuation beyond 90 days (since extended to 180 days in all areas) would be a local responsibility and most are developing their FY 1986 funding plans accordingly. It is expected that State and local health departments will assume responsibility for continuation of alternative site testing.

The primary Federal role has been to pursue knowledge about AIDS through research, surveillance and disease investigations. We believe that States and local health departments and private physicians have the responsibility to actually perform screening and provide treatment services.

Question. In your estimation, how safe is our Nation's blood supply from AIDS contamination and how accurate is our capability for identifying the existence of AIDS in the blood supply?

Answer. The blood supply is essentially safe as a result of donor exclusion guidelines and the development of tests to identify antibody to HTLV-III. The first of these tests were licensed in March 1985. Within weeks, blood banks and plasma centers throughout the country began testing all donated units, as well as inventories of blood components, to identify units that may have the virus. Currently, virtually all blood and blood components in the United States are screened, reducing the risk of transmission of HTLV-III through blood transfusion to extremely low levels.

Question. Please describe briefly CDC's public education efforts as they relate to AIDS.

Answer. Since the Spring of 1985, CDC has been operating a national hotline which answers more than 700 calls daily from the general public on AIDS and makes appropriate referrals for further information. We also awarded a total of over $1 million to 6 of the areas with the highest AIDS morbidity to conduct activities that provide risk reduction information to the public and attempt to influence the behavior of those at highest risk for AIDS. CDC has just awarded approximately $1.2 million in cooperative agreements to demonstrate the impact of current health education and risk reduction methods. Approximately $6.2 million will be used during FY 1986 to award additional demonstration projects and to initiate cooperative agreements to test innovative approaches to prevent the spread of AIDS. CDC has also developed training curriculum and educational materials, and has conducted training of health department and community personnel on the clinical and laboratory aspects of AIDS and HTLV-III infection.

In March 1985, CDC continued a cooperative agreement with the United States Conference of Mayors to help fund the grass roots AIDS health education and risk reduction efforts of 19 community-based organizations. The conference also publishes a monthly AIDS Information Exchange, which provides 800 of the nation's mayors and their local health officials with timely, accurate information about AIDS. In addition, CDC has published 65 articles in the Morbidity and Mortality Weekly Report to inform health professionals of recent AIDS findings.

In FY 1986, CDC plans to assist States in building a core capacity directed toward the prevention of AIDS and the transmission of HTLV-III infection. The States would then have the systems in place to apply known health education/risk reduction approaches and to rapidly disseminate the new prevention strategies as they are developed. In addition, approximately fifteen of the highest morbidity areas will receive funds to intensify their prevention efforts, and implement evaluation mechanisms to monitor their effectiveness.

Question. If the Committee were to determine that CDC needed additional funding for the prevention and control of AIDS, to what priority activities would you direct such funding?

Answer. One priority would be for the purchase, distribution, and evaluation of antiviral agents for the treatment of AIDS patients not included in NIH clinical trials. Once researchers determine that a drug is safe and effective in the treatment of AIDS, but before Phase III Clinical Trials have been completed, it will be important to make the drug available to those AIDS patients who cannot be enrolled in formal Clinical Trials. Once safety and efficacy is clearly demonstrated, discussions between NIH, CDC, and FDA, will ensue to make the drug available under a Treatment Investigational New Drug (IND) application. Provision of the drug by CDC will be contingent upon agreement by the institution/physician to adhere to the study protocol and provide specified information on safety and efficacy.

Question. In addition to sexual contact and blood transfusions, what other ways can AIDS be spread?

Answer. In addition to sexual contact and blood or blood products, HTLV-III has been transmitted among IV drug abusers by sharing contaminated needles. Also, babies born to mothers who have AIDS or are HTLV-III positive may become infected before, during, or immediately after birth. These methods account for the vast majority of cases in the U.S. which are not directly attributable to homosexual and heterosexual transmission. There have been two reports in the U.S. of probable transmission of AIDS virus infection to health care workers following needlestick exposure. One infant apparently acquired the infection from his mother who had acquired the infection from a transfusion after delivery.

QUESTIONS SUBMITTED BY SENATOR WILLIAM PROXMIRE

Question. Dr. Hopkins, 81 percent of the people who responded to a recent public opinion poll conducted by the Washington Post indicated that AIDS is spreading so rapidly that it is now a serious threat to the general public. Is the situation that hopeless? Do we really know how to prevent the transmission of this syndrome?

Answer. Currently, the most effective means for preventing transmission of HTLV-III are to avoid sexual contact or avoid sharing needles with infected persons. Were these two behaviors avoided, AIDS would be controlled within the duration of one incubation period of the disease. The Public Health Service's Plan for the Prevention and Control of AIDS (see Attachment 3) outlines a strategy for encouraging and supporting the adoption of behaviors which will reduce risk of transmission of HTLV-III infection and AIDS.

See attached MMWR dated January 11, 1985, for more information.

ATTACHMENT 3

Provisional Public Health Service Inter-Agency Recommendations for Screening Donated Blood and Plasma for Antibody to the Virus Causing Acquired Immunodeficiency Syndrome

In March 1983, the U.S. Public Health Service issued inter-agency recommendations on the prevention of acquired immunodeficiency syndrome (AIDS) (*1*). Included was the recommendation that members of groups at increased risk for AIDS should refrain from donating plasma and/or blood. That recommendation was made to decrease the risk of AIDS associated with the administration of blood or blood products, which accounts for about 2% of all reported AIDS cases in the United States.

Evidence has shown that a newly recognized retrovirus is the cause of AIDS. Although this virus has been given several names, including human T-lymphotropic virus type III (HTLV-III) (*2*), lymphadenopathy-associated virus (LAV) (*3*), and AIDS-associated retrovirus (ARV) (*4*), it is referred to as HTLV-III in this discussion. Tests to detect antibody to HTLV-III will be licensed and commercially available in the United States in the near future to screen blood and plasma for laboratory evidence of infection with the virus. The antibody tests are modifications of the enzyme-linked immunosorbent assay (ELISA), which uses antigens derived from whole disrupted HTLV-III (*5*).

There is considerable experience with the ELISA test in research laboratories, but much additional information will be gathered following its widespread application. In the early phases of testing, a number of false-positive tests may be encountered. Adjustments in interpretation are anticipated as more is learned about the performance of the test in an individual laboratory and about the specific proportion of falsely positive or falsely negative tests in the screening setting where the test is used.

The present recommendations concern the use of these tests to screen blood and plasma collected for transfusion or manufactured into other products. They are intended to supplement, rather than replace, the U.S. Food and Drug Administration's recently revised recommendations to blood and plasma collection facilities and the earlier inter-agency recommendations (*1*). Additional public health applications of these tests in the understanding and control of AIDS will be described in a subsequent report.

BACKGROUND

Antibody Detection Studies

The ELISA test has been used in many research programs for detecting antibodies to HTLV-III in patients with AIDS and with AIDS-related conditions. In different studies, HTLV-III antibody was found to range from 68% to 100% of patients with AIDS, and in 84%-100% of persons with related conditions, such as unexplained generalized lymphadenopathy (*5-7*). Serologic surveys have yielded variable seropositivity rates in groups at increased risk for AIDS: 22%-65% of homosexual men (*8-11*), 87% of intravenous-drug abusers admitted to a detoxification program in New York City (*12*), 56%-72% of persons with hemophilia A (*13,14*), and 35% of women who were sexual partners of men with AIDS (*15*). In contrast to the above groups, HTLV-III antibody has been detected in fewer than 1% of persons with no known risks for AIDS (*4-10*).

The time needed to develop a positive antibody test following infection is not known. Data regarding the interval between infection with HTLV-III and seroconversion are limited. A nurse who sustained a needle-stick injury while caring for an AIDS patient developed antibody between 4 and 7 weeks following exposure (*16*). Additionally, a recent study described several asymptomatic individuals infected with HTLV-III for more than 6 months in the absence of detectable antibody (*17,18*). Nonetheless, currently available ELISA tests can be expected to identify most persons with HTLV-III infection.

Virus Isolation Studies

HTLV-III has been isolated from blood, semen, and saliva and has been recovered from many individuals in the presence of antibody (*19,20*). HTLV-III has been isolated from the blood of 85% or more of seropositive individuals with AIDS (*21*), lymphadenopathy, or other AIDS-associated conditions (*2*) and from three of four mothers of infants with AIDS (*2*). The virus has also been isolated from asymptomatic seropositive homosexual men and hemophiliacs, and has been recovered from 95% of seropositive high-risk blood donors who had been implicated in the transmission of AIDS through transfusion (*21*). The recovery of HTLV-III from these high-risk donors 2 or more years after their initial donation provides evidence that viremia may persist for years in both asymptomatic and symptomatic individuals. HTLV-III has also been isolated from some asymptomatic seronegative persons, but this is the exception (*17*).

Modes of Transmission

Epidemiologic data suggest that the virus has been transmitted through intimate sexual contact; sharing contaminated needles; transfusion of whole blood, blood cellular components, plasma, or clotting factor concentrates that have not been heat treated; or from infected mother to child before, at, or shortly after the time of birth. No other products prepared from blood (e.g., immunoglobulin, albumin, plasma protein fraction, hepatitis B vaccine) have been implicated, nor have cases been documented to occur through such common exposures as sharing meals, sneezing or coughing, or other casual contact.

Natural History of Infection

Information about the course of infection with HTLV-III is incomplete, but the majority of infected adults will not acquire clinically apparent AIDS in the first few years after infection. In some studies 5%-19% of seropositive homosexual men developed AIDS within 2-5 years after a previously collected serum sample was retrospectively tested and found to be seropositive. An additional 25% developed generalized lymphadenopathy, oral candidiasis, or other AIDS-associated conditions within the same interval (*11,22*). The long-term prognosis for most persons infected with HTLV-III is unknown.

SCREENING BLOOD AND PLASMA

Initial Testing

Persons accepted as donors should be informed that their blood or plasma will be tested for HTLV-III antibody. Persons not wishing to have their blood or plasma tested must refrain from donation. Donors should be told that they will be notified if their test is positive and that they may be placed on the collection facility's donor deferral list, as is currently practiced with other infectious diseases, and should be informed of the identities of additional deferral lists to which the positive donors may be added.

All blood or plasma should be tested for HTLV-III antibody by ELISA. Any blood or plasma that is positive on initial testing must not be transfused or manufactured into other products capable of transmitting infectious agents.

When the ELISA is used to screen populations in whom the prevalence of HTLV-III infections is low, the proportion of positive results that are falsely positive will be high. Therefore, the ELISA should be repeated on all seropositive specimens before the donor is notified. If the repeat ELISA test is negative, the specimen should be tested by another test.

Other Testing

Other tests have included immunofluorescence and radioimmunoprecipitation assays, but the most extensive experience has been with the Western blot technique (*22*), in which antibodies can be detected to HTLV-III proteins of specific molecular weights. Based on available data, the Western blot should be considered positive for antibody to HTLV-III if band p24 or gp41 is present (alone or in combination with other bands).

Notification of Donors

If the repeat ELISA test is positive or if other tests are positive, it is the responsibility of the collection facility to ensure that the donor is notified. The information should be given to the donor by an individual especially aware of the sensitivities involved. At present, the proportion of these seropositive donors who have been infected with HTLV-III is not known. It is, therefore, important to emphasize to the donor that the positive result is a preliminary finding that may not represent true infection. To determine the significance of a positive test, the donor should be referred to a physician for evaluation. The information should be given to the donor in a manner to ensure confidentiality of the results and of the donor's identify.

Maintaining Confidentiality

Physicians, laboratory and nursing personnel, and others should recognize the importance of maintaining confidentiality of positive test results. Disclosure of this information for purposes other than medical or public health could lead to serious consequences for the individual. Screening procedures should be designed with safeguards to protect against unauthorized disclosure. Donors should be given a clear explanation of how information about them will be handled. Facilities should consider developing contingency plans in the event that disclosure is sought through legal process. If donor deferral lists are kept, it is necessary to maintain confidentiality of such lists. Whenever appropriate, as an additional safeguard, donor deferral lists should be general, without indication of the reason for inclusion.

Medical Evaluation

The evaluation might include ELISA testing of a follow-up serum specimen and Western blot testing, if the specimen is positive. Persons who continue to show serologic evidence of HTLV-III infection should be questioned about possible exposure to the virus or possible risk factors for AIDS in the individual or his/her sexual contacts and examined for signs of AIDS or related conditions, such as lymphadenopathy, oral candidiasis, Kaposi's sarcoma, and unexplained weight loss. Additional laboratory studies might include tests for other sexually transmitted diseases, tests of immune function, and where available, tests for the presence of the virus, such as viral culture. Testing for antibodies to HTLV-III in the individual's sexual contacts may also be useful in establishing whether the test results truly represent infection.

RECOMMENDATIONS FOR THE INDIVIDUAL

An individual judged most likely to have an HTLV-III infection should be provided the following information and advice:

1. The prognosis for an individual infected with HTLV-III over the long term is not known. However, data available from studies conducted among homosexual men indicate that most persons will remain infected.
2. Although asymptomatic, these individuals may transmit HTLV-III to others. Regular medical evaluation and follow-up is advised, especially for individuals who develop signs or symptoms suggestive of AIDS.
3. Refrain from donating blood, plasma, body organs, other tissue, or sperm.
4. There is a risk of infecting others by sexual intercourse, sharing of needles, and possibly, exposure of others to saliva through oral-genital contact or intimate kissing. The efficacy of condoms in preventing infection with HTLV-III is unproven, but the consistent use of them may reduce transmission.
5. Toothbrushes, razors, or other implements that could become contaminated with blood should not be shared.
6. Women with a seropositive test, or women whose sexual partner is seropositive, are themselves at increased risk of acquiring AIDS. If they become pregnant, their offspring are also at increased risk of acquiring AIDS.
7. After accidents resulting in bleeding, contaminated surfaces should be cleaned with household bleach freshly diluted 1:10 in water.
8. Devices that have punctured the skin, such as hypodermic and acupuncture needles, should be steam sterilized by autoclave before reuse or safely discarded. Whenever possible, disposable needles and equipment should be used.
9. When seeking medical or dental care for intercurrent illness, these persons should inform those responsible for their care of their positive antibody status so that appropriate evaluation can be undertaken and precautions taken to prevent transmission to others.
10. Testing for HTLV-III antibody should be offered to persons who may have been infected as a result of their contact with seropositive individuals (e.g., sexual partners, persons with whom needles have been shared, infants born to seropositive mothers).

Revised recommendations will be published as additional information becomes available and additional experience is gained with this test.

Reported by Centers for Disease Control; Food and Drug Administration; Alcohol, Drug Abuse, and Mental Health Administration; National Institutes of Health; Health Resources and Services Administration.

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Question. Dr. Hopkins, I understand local health officials are very supportive of alternative screening sites and increasing numbers of health departments are encouraging at-risk groups to use these sites not only as a diagnostic source but as a contact point for receiving accurate information about AIDS prevention. Why hasn't CDC requested any funds to continued this activity?

Answer. CDC awarded funds in April with the clear purpose of underwriting the initial development of alternative sites and a laboratory capability for their support. The primary Federal role has been to pursue knowledge about AIDS through research, surveillance and disease investigations. We believe that States and local health departments and private physicians have the responsibility to actually perform screenings and provide treatment services. All grantees understood that continuation beyond 90 days (since extended to 180 days in all areas) would be a local responsibility and most are developing their FY 1986 funding plans accordingly. It is expected that State and local health departments will assume responsibility for continuation of alternative site testing.

Question. Dr. Hopkins, I'm hoping you can clarify something for me regarding the cooperative agreements which I understand CDC will initiate with each of the 50 States in order to implement the Community health education and risk reduction program. What I have a problem with is the $125,000 ceiling and $75,000 floor established by CDC as funding set points in the agreement. $125,000 won't go very far in States such as New York and California which have high percentages of AIDS victims. How did you arrive at these levels?

Answer. That range was derived from estimating that approximately $100,000 is needed to establish a basic capability to do well planned AIDS health education and risk reduction, and then assuming that costs would vary by about 25 percent from one area of the country to another. The estimate was based on the cost of a coordinating person with health education credentials, clerical and statistical support, travel expenses and the need to conduct surveys of segments of the community for the purpose of establishing an educational diagnosis of the local AIDS problem. These surveys are designed to establish a baseline of information about AIDS knowledge in various segments of the community and identify the scope of certain behaviors and/or sexual practices among groups and individuals at particular risk for AIDS. From this information a carefully targeted health education and risk reduction program can then be developed.

In addition, these funds to States will be augmented by awards totalling approximately $7.8 million to fifteen cities with the highest morbidity, to intensify their prevention efforts and implement evaluation mechanisms to monitor their effectiveness.

Question. How are States which have no AIDS cases treated under the agreement? Are they still eligible for the minimum amount of $75,000?

Answer. Yes, States with no AIDS cases are eligible for the minimum amount of $75,000. CDC believes that every State needs a health education and risk reduction program for several basic reasons. First, while it is true that not every State has yet reported a case of AIDS, this clinical diagnosis represents a small fraction of the potential for morbidity associated with HTLV-III infection. For example, it is estimated that nearly 100,000 people in the United States have AIDS related conditions, and that another 500,000 to 1 million individuals are infected with the virus, but are clinically well at present. It is presumed that each of these individuals has some chance of developing clinical AIDS, spreading the virus to others, or both. Historic efforts to control other communicable diseases with epidemiologic patterns resembling AIDS suggest the prudence of establishing a preventive effort in low morbidity areas.

The second reason is that a program of health education and risk reduction is the only preventive measure currently available to reduce transmission among individuals at risk. At present, the control of AIDS is dependent upon whether or not individuals at risk learn about behaviors that will minimize spread, adopt those behaviors, and receive the reinforcement to sustain the change. Therefore, developing such core capacity soon is imperative.

Thirdly, States with few (or no) reported cases represent our best opportunities for prevention since there is less risk of exposure to HTLV-III infection than in States with larger numbers of cases.

And lastly, we live in an age of tremendous mobility within and across State lines. Since the risk of HTLV-III transmission crosses county and State boundaries, all States must possess the capacity to work actively to prevent and control transmission within their borders.

Question. Does the agreement spell out how these particular States should use the funds?

Answer. The funds are intended to assist States in appraising community needs and resources related to the AIDS problem and to assist States in strengthening their capacity to deliver health education and risk reduction programs. It is expected that the following kinds of activities will be carried out:

- o Assess community needs and resources concerning AIDS prevention among high-risk groups and in the general population.
- o Determine the levels of disease-related knowledge, attitudes and behaviors among persons at risk of infection.
- o Strengthen the organized collaboration of community level resources directed toward the prevention of AIDS and the transmission of HTLV-III infection.
- o Deliver health education/risk reduction services that are specifically targeted to groups and individuals known to have risk factors for AIDS.

Question. Just one final question regarding these cooperative agreements, Dr. Hopkins. Is the District of Columbia and Puerto Rico included?

Answer. Yes. Eligible applicants are the official public health agencies of States, including the District of Columbia, the Commonwealth of Puerto Rico, the Virgin Islands, Guam, the Trust Territory of the Pacific Islands, the Northern Mariana Islands, and American Samoa.

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

QUESTIONS SUBMITTED BY THE SUBCOMMITTEE

Question: Dr. Macdonald, I understand a supplemental request from the Alcohol, Drug Abuse, and Mental Health Administration for AIDS research is currently under consideration by the Public Health Service. What is the amount of the supplemental currently being considered?

Answer: The total amount of the AIDS supplemental requested for 1986 is $9.2 million.

Question: Specifically, what initiatives will be undertaken with the proposed supplemental funds?

Answer: The National Institute on Drug Abuse proposes to:

- Continue to clarify the epidemiology and natural history of HTLV-III infection in IV drug users. In addition, NIDA will recommend that drug abuse treatment programs commence case finding and referral efforts in order to identify drug users with AIDS, or at high risk for contracting and/or spreading the HTLV-III virus.

- Stimulate and conduct research and development of effective prevention approaches and treatment agents. NIDA focuses its efforts on research related to HTLV-III disease among the drug-using population. In addition to epidemiologic studies (e.g., etiology, risk factors, and natural history), NIDA will expand research on effective prevention and intervention strategies to determine their efficacy in reducing the spread of HTLV-III diseases among the drug-using population.

- Continue to implement national, state, and community risk prevention and education programs as prevention and control measures. NIDA will continue to develop and disseminate information aimed at reducing the incidence of HTLV-III and disseminate information to specific high risk subgroups and the general public about the relationship between drug abuse, the spread of HTLV-III, and the subsequent development of AIDS/ARC.

- Design and evaluate improved prevention and control measures. NIDA will expand its knowledge transfer and technical assistance activities aimed at better informing drug abuse treatment providers about methods and procedures most suited for serving drug abuse clients infected with, or at-risk for HTLV-III disease. Efforts will be aimed at engaging in drug abuse treatment, and/or other appropriate medical programs for drug users who are infected with AIDS/ARC or at high risk of contracting and/or spreading HTLV-III infections. Because there are significant geographic differences in the incidence of AIDS among IV drug users, control programs recommended may vary from state to state.

In addition, the National Institute of Mental Health proposes to:

- Clarify the epidemiology and natural history of HLTV-III infection by continuing to support investigations of mental health risk factors as they relate to the incidence of AIDS. Because of the limited knowledge currently available regarding mental health aspects of AIDS, ARC and HTLV-III exposure, NIMH will continue to provide research support for projects focused on the psychiatric, biobehavioral, neuropsychologic, and psychosocial aspects of AIDS. Areas of additional needed emphasis include: research on the neuropsychiatric and neuropsychological factors involved in HTLV-III infection to assess differences between psychological reactions to the disease and organic problems resulting from the disease process which may also affect mood, cognition, development and behavior; the development and testing of psychological and behavioral measures to assess mental health status as it relates to AIDS; psychological reactions to receiving a positive or negative result on the HTLV-III blood test; and the interplay between psychoactive drugs and immune function.

- Continue to implement national, state, and community risk prevention and education programs as early prevention and control measures. NIMH will continue to develop and disseminate information to the general public on mental health consequences of AIDS. In addition, the Institute proposes to increase research and dissemination efforts toward specific population groups, such as health care providers (including physicians, primary care residents, psychiatry residents, nurses, volunteers in the community/city/county/state, blood bank staff), and community-based AIDS organizations. The information to be conveyed will include dissemination of knowledge relative to psychological and psychosocial issues related to those in high risk groups, those in contact with AIDS patients, and those with AIDS/ARC as well as the medical/psychiatric complications of HTLV-III and their clinical manifestation such as delirium and dementia. These dissemination activities will be accomplished through a variety of mechanisms including press, media, and national professional association contacts and efforts to work with local radio and television to develop education programs for the general public.

- Design and evaluate improved prevention and control measures. Consideration needs to be given to establishing a high level group of advertisers, opinion change experts, and PHS health education experts to recommend effective messages and strategies. NIMH will develop a plan for establishing an advisory group for public information and education strategies, for discussion with the Public Information Panel and possible consideration by the PHS Executive Task Force on AIDS.

Question: How many additional full-time equivalent positions will be needed to carry out the activities proposed in the supplemental request?

Answer: Seven full-time equivalent positions are being requested -- three for the National Institute of Mental Health and four for the National Institute on Drug Abuse. In both Institutes, the additional positions would be used to carry out the research, technical assistance and information dissemination activities proposed by each.

Research on AIDS and Intravenous Drug Use

Question: It is my understanding that NIDA has blood samples taken from intravenous drug users from the early 1970s which are now being tested for the AIDS virus.

* What do the results of these tests indicate with regard to the prevalence of the virus among this population?

* Does NIDA intend to conduct a follow-up study of these drug users to determine whether they have developed the disease?

* What information could be gained by conducting such a study, and what do you estimate it would cost?

Answer: Blood samples gathered from IV drug-using patients and controls during the early 1970s are presently being tested by state of the art technology for the presence of HTLV-III antibody and virus. Results from this work are not yet available. The objective of this work is not to measure the magnitude of the prevalence of HTLV-III infection in these samples, but rather to ascertain when the infection first presented in the IV drug-using population. If seropositive individuals for HTLV-III were confirmed in this sample, it would alter the theoretical framework of how and when the disease entered this country.

If there are confirmed cases of HLTV-III infection identified, NIDA does intend to proceed with follow-up research. Attention will be given to ensuring confidentiality in attempting to locate subjects or otherwise obtain information about them (e.g., from death records). Follow-up studies would provide important additional information on conversion from HTLV-III test positive to the development of AIDS. The cost of such research is tied to the number of patients needing follow-up and cannot be estimated at this time.

Question: Has there been any coordinated effort both within ADAMHA, and in conjunction with the other agencies of the Public Health Service, to develop a policy with regard to public education about AIDS?

- Have you given any consideration to using clinical training funds to have university departments of psychiatry or psychology develop training programs for health care providers so that they are aware of, and can address, the mental health problems of AIDS patients?

Answer: In response to the PHS Plan to Prevent and Control AIDS, ADAMHA has developed strategies to provide public education about AIDS. These include documents directed toward health care providers concerning the psychosocial aspects of AIDS, toward the drug treatment worker concerning issues of AIDS relevant to addiction, and toward the IV drug user. These publications have been developed in collaboration with other PHS agencies.

ADAMHA has developed plans to establish educational programs within competitively selected medical schools to make health care providers aware of the psychosocial issues for AIDS patients, and these are under review.

FOOD AND DRUG ADMINISTRATION

Questions Submitted by the Subcommittee

Use of HPA-23

We are hearing of United States citizens who fly to Paris to obtain HPA-23 or to other countries to purchase isoprinosine or ribavirin.

Q. Why can't these drugs be obtained in this country?

A. HPA-23, isoprinosine and ribavirin are now available in this country as experimental drugs for treating patients with

AIDS or AIDS-related illnesses. Until these studies are completed, the results reviewed, and a determination made regarding their effectiveness in treating these conditions, they can not be obtained commercially in this country.

The Food and Drug Administration (FDA) has been extremely sensitive to the AIDS problem and has expedited all requests for the study of experimental drugs for AIDS. Requests for the investigational study of isoprinosine, HPA-23 and ribavirin have been received and approved by the FDA. HPA-23 has also been made available for a small number of Americans who had received the drug on a regular basis in France.

When data are available to support the safety and efficacy of any drug intended for treatment of AIDS, FDA reviews it expeditiously. It should be noted that some of the drugs being developed have already been found to have significant toxicity and may cause severe irreversible adverse affects. Consequently, studies must begin with a small number of patients intensively monitored by qualified expert investigators to assure patient safety; they then will be gradually enlarged as we become more knowledgeable in how to use the drug and preliminary safety and efficacy data are obtained.

Q. Can you review for us how many drugs have been shown to have antiviral activity against the AIDS virus?

A. A number of drugs have been shown to have antiviral activity against the HTLV-III virus in the laboratory including: ribavirin, phosphonoformate, suramin, BW A509U, ansamycin, and HPA-23. Of these, FDA has approved experimental human studies with all but ansamycin and phosphonoformate; however, we are discussing such studies with their respective manufacturers and expect them to begin soon.

Q. Where and how do you plan to test them?

A. Clinical trials are normally conducted at medical centers by qualified investigators who have the scientific capability of making observations regarding the safety of the drugs, the effects of the drug on virus replication, and the effects of the drug on the manifestations of the disease. The Clinical Center at the National Institutes of Health (NIH) is conducting such clinical trials as are a number of other medical centers, particularly in cities with large high-risk populations. The NIH generally sponsors its own trials; trials in other locations are being sponsored by NIH, pharmaceutical companies, or individual investigators. It is anticipated that the number of institutions involved in clinical studies will continue to expand.

Q. Do you feel that the drugs that are currently tested for antiviral activity against the AIDS virus or drugs that will be tested should be made available to every person with AIDS who wants some type of treatment, even if it is still in the experimental form?

A. We believe that it is in the interest of the public health as well as the patients that any AIDS-patient who is interested in being treated with an experimental drug be enrolled in a scientifically sound clinical study and monitored by a qualified expert to assure their safety to the maximum extent possible. The advantages to the patient involve safety and optimum medical care. The advantage to society is that this approach has been shown to be the most rapid and efficient means of demonstrating a drug's usefulness, and for developing a proper method for using the drug. When it has been determined that a drug is demonstrated to have some clinical benefit for patients, it is the Public Health Service's intent to make these drugs more widely available.

Q. What effect would making drugs available in this manner to everyone have on the outcome of controlled clinical trials?

A. The normal course of drug development is to proceed from small, intensively monitored studies at a limited number of locations to larger trials involving more patients and/or more locations. This approach speeds the acquisition of data received for the drug's eventual approval for general use and minimizes the risk for patients. We would encourage any patient who is interested in being treated with an experimental drug to discuss with their physician the possibility of being included in a clinical trial. Any other use of the drugs at this time is neither safe nor useful and would make their development more prolonged.

QUESTIONS SUBMITTED BY SENATOR WILLIAM PROXMIRE

Q. Dr. Young, I notice in the documents which accompanied the budget amendment tht part of the $2.9 million requested by your Agency would be used to - and I quote - CLARIFY THE POSSIBLE TRANSMISSIBILITY OF AIDS THROUGH FOOD. Can you tell us more about this?

A. At the time when we were developing the budget last summer, our philosophy on AIDS research was that we should pursue all avenues of research because, at that time, we were still unsure of all the ways that AIDS could be transmitted. However, since that time there has been substantial epidemiologic evidence developed through studies of families of AIDS patients as well as other recently provided biological evidence showing that AIDS is not likely to be transmitted through foods. Although for this reason, the research contract on the transmissibility of AIDS through food which was cited in our budget materials last September has been diverted to other AIDS research, the FDA will continue to monitor and evaluate the increasing body of evidence on this disease and will explore other research approaches to this issue of transmission in foods to assure the safety of the food supply.

Memorandums From John C. Petricciani, M.D., Director, Office of Biologics, National Center for Drugs and Biologics, Food and Drug Administration

March 21, 1983

FROM: Director, Office of Biologics,
National Center for Drugs and Biologics

SUBJECT: Recommendations to Decrease the Risk of Transmitting
Infectious Diseases from Blood Donors

TO: All Establishments Collecting Human Blood for Transfusion.

The Acquired Immune Deficiency Syndrome (AIDS) has caused serious concern among members of the blood banking community because of the implications for transfusion recipients if this disease is proven to be transmissible by blood or blood products. The major organizations engaged in blood collection have recently reached a consensus as to steps which should be taken to decrease the risk of transmitting infectious diseases by blood transfusion. Consistent with the recommendations of the American Red Cross, the American Association of Blood Banks, the Council of Community Blood Centers, the Public Health Service Interagency Committee (copy attached), the Office of Biologics is advising all establishments collecting blood for transfusion to institute additional measures designed to decrease blood collection from individual donors and donor groups known to be at increased risk for transmitting infectious diseases. The following steps should be included:

1. Educational programs should be instituted to inform persons at increased risk of AIDS (as presently defined: persons with symptoms and signs suggestive of AIDS, sexually active homosexual or bisexual men with multiple partners, Haitian entrants to the United States, present or past abusers of intravenous drugs* and sexual partners of individuals at increased risk of AIDS) that until the AIDS problem is resolved or definitive tests become available, they should refrain from blood donation because of the potential risk to recipients of their blood. Educational programs should include the individual donor as a part of the donor screening procedure.

2. Re-education of personnel responsible for donor screening should be conducted with special attention to recognition of the early signs and symptoms of AIDS. The donor medical history should include specific questions designed to detect possible AIDS symptoms or exposure to patients with AIDS. Standard Operating Procedures (SOP) should be revised to include questions which elicit a history of night sweats, unexplained fevers, unexpected weight loss, or signs of lymphadenopathy or Kaposi's sarcoma.

3. Re-education of personnel responsible for donor screening should be conducted with special attention to identifying the early signs and symptoms of AIDS in donors. The donor medical history should include specific questions designed to detect possible AIDS symptoms or exposure to patients with AIDS. Standard Operating Procedures (SOP) should be revised to include questions which elicit a history of night sweats, unexplained fevers, unexpected weight loss, or signs of lymphadenopathy or Kaposi's sarcoma.

4. Donors should be examined for lymphadenopathy. The initial and annual physical should provide an opportunity for an examination by the physician for generalized lymphadenopathy, while a more limited

*Such drug abusers are already excluded by existing regulations.

examination should be performed by an adequately trained individual on each donor on the day of plasma collection and a record made of the results of the examination.

5. An accurate record of each source plasma donor's weight prior to each donation should be made to permit ready identification of any unexplained weight loss. Any significant, unexplained decrease in weight should be considered cause for referral of the donor to a physician for complete evaluation prior to any further plasma collection. Any plasma in storage, which was previously collected from such a donor, should be quarantined until the physician's evaluation is completed.

6. The SOP should inform the staff that any products collected from a donor known or suspected to have AIDS should be considered potentially highly infectious and must be immediately quarantined and disposed of expeditiously and appropriately unless designated for investigative use related to AIDS. If not destroyed, such products must be labeled, stored and shipped in accordance with the standard procedures for handling infectious materials. Appropriate disposal procedures include autoclaving or controlled incineration; overwraps are required to protect staff in case of breakage.

Approved procedures developed by one of the major organizations such as the American Blood Resources Association, the American Red Cross, the American Association of Blood Banks and the Council of Community Blood Centers may be referenced in the licensed establishment's SOPs without individual submission to the Office of Biologics. Alternatively, licensed establishments which develop their own procedures should submit them to the Office of Biologics for approval concurrent with implementation. Revised labeling for plasma collected from high risk donor groups and intended for further manufacture of plasma derivatives should be submitted to the Office of Biologics (HFN-825).

This memorandum is intended to be an interim measure to protect recipients of blood and blood products until specific laboratory tests are available.

John C. Petricciani, M.D.

John C. Petricciani, M.D.

March 24, 1983

FROM: Director, Office of Biologics,
National Center for Drugs and Biologics

SUBJECT: Recommendations to Decrease the Risk of Transmitting Acquired Immune Deficiency Syndrome (AIDS) from Plasma Donors

TO: All Establishments Collecting Source Plasma (Human)

The Acquired Immune Deficiency Syndrome (AIDS) has caused serious concern because of the implications for recipients of plasma derivatives if this disease is proven to be transmissible by blood or blood products. The major organizations involved in plasma collection have reached a consensus as to appropriate steps which should be taken to decrease the potential of blood or plasma donation by individuals who might be at increased risk of transmitting AIDS. Consistent with the recommendations of the American Blood Resources Association, the American Red Cross, the American Association of Blood Banks, the Council of Community Blood Centers, and the Public Health Service Interagency Committee, (copy attached),

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*Such intravenous drug abusers are already excluded by existing regulations.

the Office of Biologics is advising that the following steps should be taken by all establishments collecting Source Plasma (Human):

1. Educational programs should be instituted to inform persons at increased risk of AIDS that until the AIDS problem is resolved or definitive tests become available, they should refrain from routine plasma donation because of the potential risk to recipients of certain plasma derivatives. As presently defined, persons at increased risk include those with symptoms and signs suggestive of AIDS, sexually active homosexual or bisexual men with multiple partners, Haitian entrants to the United States, present or past abusers of intravenous drugs* and sexual partners of individuals at increased risk of AIDS. Each Source Plasma donor should receive information about AIDS including the need for individuals at increased risk to voluntarily exclude themselves from routine plasma programs.

2. If plasma is collected from a donor belonging to any of the groups at increased risk, a label should be affixed to each unit to restrict its use in accordance with 21 CFR 606.120(b)(6). The recommended label statements are "CAUTION: For Use in Manufacturing Albumin, PPF, or Globulin Only" or "CAUTION: For Use in Manufacturing Noninjectable Products Only". HBsAg positive plasma is already subject to special labeling and shipping restrictions and these programs are not affected by this memorandum.

3. The SOP should specifically inform staff that all blood or blood products inadvertently collected, or collected for therapeutic purposes, from a donor known or suspected of having AIDS should be considered highly infectious and must be immediately quarantined and disposed of expeditiously unless designated for investigative use related to AIDS. If not destroyed, such products must be labeled, stored and shipped in accordance with the standard procedures for handling bio-hazardous materials. Appropriate disposal procedures include autoclaving or controlled incineration; overwraps are required to protect staff in case of breakage.

Approved procedures developed by one of the major organizations such as the American Red Cross, American Association of Blood Banks, Council of Community Blood Centers and American Blood Resources Association may be referenced in the licensed establishments' SOP without individual submission to the Office of Biologics. Alternatively, licensed establishments should develop their own procedures and should submit them directly to the Office of Biologics for approval concurrent with implementation.

This memorandum is intended to be an interim measure to protect recipients of blood and blood products until specific laboratory tests are available.

John C. Petricciani, M.D.
John C. Petricciani, M.D.

March 24, 1983

FROM: Director, Office of Biologics,
National Center for Drugs and Biologics

SUBJECT: Source Material Used to Manufacture Certain Plasma Derivatives

TO: All Licensed Manufacturers of Plasma Derivatives

Extensive discussions among licensed manufacturers, the Office of Biologics and concerned groups such as the National Hemophilia Foundation, have led to a consensus concerning an appropriate approach to decreasing the potential risk of transmitting Acquired Immune Deficiency Syndrome (AIDS) by certain plasma derivatives.

Plasma collected from donors suspected of being at increased risk of transmitting AIDS (as presently defined: persons with symptoms and signs suggestive of AIDS, sexually active homosexual or bisexual men with multiple partners, Haitian entrants to the United States, present or past abusers of intravenous drugs* and sexual partners of persons at increased risk of AIDS) should not be fractionated into derivatives already known to have a risk of transmitting infectious diseases. Plasma from donors in any of the groups identified above may be collected for use in manufacturing only albumin, plasma protein fraction (PPF), globulin or in vitro diagnostic products. To prevent the possible misuse of such plasma, all licensed establishments collecting Source Plasma (Human) are being advised that in accordance with 21 CFR 606.120(b)(6) each unit must be conspicuously labeled either with the statement "CAUTION: For Use in Manufacturing Albumin, PPF, or Globulin Only," or "CAUTION: For Use in Manufacturing Noninjectable Products Only". HBsAg positive plasma for use in manufacturing vaccine or in vitro diagnostic products is already subject to additional special labeling and shipping precautions.

We request that you immediately institute procedures with your plasma suppliers to assure that they have adopted appropriate donor screening practices and procedures. Copies of notices that are being sent to all establishments collecting blood or source plasma concerning measures which should be taken, are enclosed for your information along with the recent Public Health Service Interagency Recommendations.

Please advise the Office of Biologics, in writing, of the procedures you have instituted to comply with this notice. The restrictions applied by your establishment on source plasma received for manufacturing high risk plasma derivatives should be effective immediately.

John C. Petricciani, M.D.
John C. Petricciani, M.D.

Memorandums From Elaine C. Esber, M.D., Acting Director, Office of Biologics Research and Review, Food and Drug Administration

December 14, 1984

FROM: Acting Director, Office of Biologics Research and Review

SUBJECT: Revised Recommendations to Decrease the Risk of Transmitting Acquired Immunodeficiency Syndrome (AIDS) from Blood and Plasma Donors

TO: All Establishments Collecting Blood, Blood Components or Source Plasma and all Licensed Manufacturers of Plasma Derivatives

On 24 March 1983, we issued recommendations to decrease the risk of transmitting the Acquired Immunodeficiency Syndrome (AIDS) from blood and plasma donors. Recently the HTLV-III virus has been reported as the etiologic agent of AIDS, and government and industry are proceeding as rapidly as possible with the development of a laboratory screening test for antibody to the virus. However, we believe it is still very important to continue to apply interim measures to prevent the collection of blood or plasma from individuals who might be at increased risk of transmitting

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*Such intravenous drug abusers are already excluded by existing regulations.

AIDS. The purpose of this memorandum is to provide you with a revised set of recommendations based on a number of suggestions which have been received since March 1983. The desirability of revising the recommendations was discussed at a public workshop held on June 6th with participation by representatives of FDA's Blood Products and Vaccine Advisory Committees, the Centers for Disease Control, the blood and plasma industries, and the American Association of Physicians for Human Rights. There was general agreement at the workshop that the recommendations should be revised to address several areas that were ambiguous or on which more specific guidance would be helpful. The attached recommendations reflect those suggestions, and we are requesting your cooperation in adopting these updated recommendations at the earliest possible time.

All of the basic principles of donor screening remain unchanged; only minor alterations in operating procedures will be required. It will not be necessary for each licensed establishment to submit updated SOPs for our files. The FDA field investigators will confirm during routine inspections that appropriate procedures are being applied. We are confident that you share our concern for the safety of blood products and plasma derivatives, and that you will want to use the most effective means available to prevent the transmission of AIDS.

Elaine Esber

Elaine C. Esber, M.D.

INTERIM PROCEDURES TO MINIMIZE THE RISK OF TRANSMITTING AIDS THROUGH BLOOD PRODUCTS OR PLASMA DERIVATIVES:

1. Educational materials should be provided to inform donors that at this time the following individuals should refrain from donating blood or plasma.

   A. Anyone who has AIDS or one of its signs and symptoms which include: unexplained weight loss; night sweats; blue or purple spots typical of Kaposi's sarcoma on or under the skin, or on mucous membranes; swollen lymph nodes lasting more than one month; persistent white spots or unusual blemishes in the mouth; fever >99° F for more than 10 days; persistent cough and shortness of breath; persistent diarrhea.

   B. Past or present abusers of intravenous (IV) drugs.

   C. Males who have had sex with more than one male since 1979, and males whose male partner has had sex with more than one male since 1979.

   D. Haitians who have entered the U.S. after 1977. Note: All persons who have resided in Haiti are deferred from blood donation for three years after leaving the country because of the risk of transmitting malaria by the transfusion of red cells.

   E. Patients with hemophilia.

   F. Sexual partners of individuals in any of the above categories.

   Exceptions to this recommendation should be discussed individually with the Division of Blood and Blood Products (Mrs. Ann Hoppe, 301-496-4396). For example, blood or plasma from categories A-F above may be needed for research reagents related to AIDS or other diseases. Facilities already approved to collect plasma from donors with hemophilia need only submit a letter to the Office of Biologics Research and

Review stating that such plasma will be restricted to in vitro coagulation studies.

2. The medical screening of blood and plasma donors should include specific questions concerning a history of night sweats, unexplained fevers, unexpected weight loss, persistent cough or shortness of breath, white spots or unusual blemishes in the mouth, persistent diarrhea or signs of lymphadenopathy or Kaposi's sarcoma. The donor's response to these questions should be recorded as part of the determination of donor suitability (21 CFR 640.3 and 640.63).

   Additional requirements for Source Plasma:

   A. Source plasma donors should be examined for lymphadenopathy. The initial and annual physical examination should provide an opportunity for an examination by the physician for generalized lymphadenopathy. A more limited examination for cervical lymphadenopathy should be performed on each donor by an adequately trained individual on each day of plasma collection and a record made of the results of the examination.

   B. The existing cumulative records of each source plasma donor's weight should be examined to assure that any weight loss of 10 pounds or more in less than two months is detected. Donors with unexplained weight loss must be referred to a physician for complete evaluation prior to any further plasma donation.

3. To increase the effectiveness of voluntary self-exclusion procedures for individuals who may be at increased risk of transmitting AIDS, all establishments collecting blood or plasma should provide a confidential means whereby the donor can prevent his or her blood or plasma from being used for transfusion or for the preparation of plasma derivatives. An acceptable procedure now being used in some centers is to have every donor complete a confidential form, linked to the donor only by unit number, that designates whether the blood or blood component can be used for transfusion or further manufacturing into plasma derivatives, or whether it should be restricted for special laboratory studies. Alternatively, in situations where a physician is present at the collection facility, an opportunity could be provided for the physician to instruct each donor, in a private setting such as during a physical exam, on the importance of individuals who are at increased risk of AIDS to refrain from donating. Such a procedure should allow donors the opportunity to self-exclude in a confidential manner.

4. The following special precautions apply when it is learned that a donor has developed AIDS, or signs or symptoms of AIDS. The SOP should inform the staff that products or samples collected from a donor who has developed AIDS, or signs and symptoms of AIDS, should be quarantined immediately. Such products or samples must be labeled and stored or shipped in accordance with the standard procedures for handling infectious materials. The products may be held in quarantine pending clarification of the donor's diagnosis, or they may be designated for investigative use related to AIDS. The Division of Blood and Blood Products (Mrs. Ann Hoppe, 301-496-4396) should be notified of such instances, and guidance regarding the further evaluation of the donor and the disposition of products may be given at that time. Appropriate disposal procedures include autoclaving or controlled incineration; overwraps are required to protect staff in case of breakage.

September 3, 1985

FROM: Director, Office of Biologics Research and Review

SUBJECT: Revised Definition of High-Risk Groups With Respect to Acquired Immunodeficiency Syndrome (AIDS) Transmission from Blood and Plasma Donors

TO: All Registered Blood Establishments

The purpose of this memorandum is to provide a new statement to immediately replace item 1.C., of our 14 December 1984 memorandum concerning donor exclusion criteria. Item 1.C. should be modified to read as follows:

1. C. ANY MALE WHO HAS HAD SEX WITH ANOTHER MALE SINCE 1977.

This includes even those individuals who have had only a single homosexual experience and may not regard themselves as homosexual or bisexual.

Our previous memoranda of 24 March 1983 and 14 December 1984 provided recommendations to decrease the risk of transmitting AIDS from blood and plasma donors. Included in these Recommendations were measures to prevent the collection of blood or plasma from individuals at increased risk of transmitting AIDS. These early definitions of risk groups were based primarily upon AIDS epidemiologic data and were intended to make blood products safer by excluding donors who were more likely to be infected with the causative agent, human T-lymphotropic virus type III (HTLV-III). Although all blood and plasma can now be tested for HTLV-III antibodies, and units found to be repeatedly reactive are routinely eliminated from use for transfusion or further manufacture into injectable products capable of transmitting infectious agents, appropriate donor selection continues to provide an additional important safeguard.

The low prevalence of confirmed positive HTLV-III antibody tests in blood donors suggests that voluntary deferral has been highly effective. However, the very rapid accumulation of data since the initial HTLV-III antibody test was licensed in March 1985 has facilitated the re-evaluation of donor criteria, and has permitted the first objective assessment of the effectiveness of donor education efforts. Many of the relevant data were presented at the 31 July 1985 workshop in Bethesda, MD, sponsored by the Food and Drug Administration, the Centers for Disease Control and the National Institutes of Health. Following this workshop, the major blood and plasma collecting organizations and the Public Health Service have discussed donor selection criteria and have concluded that the data now available mandate the uniform application of a significantly more straightforward criterion related to males who have had sex with another male. In brief, the change in risk group definition is prompted by the discovery that the majority of interviewed individuals having confirmed positive HTLV-III test results have been homosexual or bisexual males who felt that they were not in a risk group. The report of 1,027,786 antibody tests on blood donors in American Red Cross Blood Services (New England Journal of Medicine 313:384, August 8, 1985) provides detailed information in support of the revised recommendation.

In addition, the availability of a serologic test which has allowed the evaluation of libraries of stored sera has provided a more accurate determination of the time at which this virus began spreading in the U.S. homosexual population. Based on this new information, the time frame for exclusion of homosexual and bisexual males has been changed from 1979 to 1977; this period is also consistent with the continuing criterion for Haitian immigrants.

Please note that the educational materials used to inform donors concerning the risk of transmitting AIDS should clearly convey the fact that all males who have had sex with another male since 1977 should refrain from donating blood or plasma. This includes even individuals who have had only a single homosexual experience and may not regard themselves as homosexual or bisexual. It is particularly important to communicate this message to bisexual males (and their sexual partners) because they may not have had access to the health-related educational information readily available to much of the gay community.

We recognize that the printing of educational materials requires a reasonable time period, but you are urged to immediately implement the new criterion by means of an addendum highlighting this change. The new wording will be included in an updated comprehensive summary of all AIDS related recommendations for blood establishments, which will be distributed in the near future.

Questions concerning the revised recommendation may be addressed to any of the members of the HTLV-III working group.

Madge L. Crouch
for Elaine C. Esber, M.D.

NONDEPARTMENTAL WITNESSES

STATEMENTS OF:

DR. WILLIAM A. HASELTINE, HARVARD UNIVERSITY

DR. MALCOLM A.S. MOORE, MEMORIAL SLOAN-KETTERING CANCER CENTER

DR. DON C. DES JARLAIS, NEW YORK STATE DIVISION OF SUBSTANCE ABUSE

PREPARED STATEMENTS

Senator WEICKER. Our first witness is Dr. William Haseltine, chief, laboratory of biomedical pharmacology, Dana-Farber Cancer Institute, Harvard.

Dr. HASELTINE. Mr. Chairman, I am going to limit my remarks to a summary of what I have submitted. I would appreciate it if you could enter the text of the testimony as well as addendums. One is a question and answer, commonly asked questions and answers on the subject of AIDS. In a similar format, a second is a description of myths and answers to those myths and, third, is something called a battleplan for the fight against the AIDS.

Senator WEICKER. Your statement and the various addendums along with the statements accompanying you will be included in the record in their entirety at this point.

[The statements follow:]

[CLERK'S NOTE.—A revised statement submitted by Dr. William Haseltine has been received and is being retained in the subcommittee files.]

Statement of Dr. William A. Haseltine

We are now engaged in another deadly episode in the historic battle of man versus microbe. These battles have shaped the course of human evolution and of history. We have seen the face of our adversary in this case a tiny virus that causes AIDS. We have yet to take its full measure. We now know it by the havoc it wreaks upon the immune system defenses and the brain. The epidemic is worldwide. To this battle we bring the strength that we have as human beings, the ability to communicate, to organize, and to think. We also bring to this fight our accumulated hard won knowledge embodied in our biomedical community. What I am here today to tell you is something about the scope of the problem, what we have learned about this new disease AIDS, and most importantly, how much more we still must do. I will urge you to help us marshall our resources to stem this deadly epidemic.

From our current vantage point, it seems as if this disease appeared in our midst as some unwanted guest, suddenly and without warning. In this country alone, well over one million people are now carriers of this virus, and to the best of our knowledge, most of these people will remain carriers for life. About one hundred thousand of those people infected with the virus in the United States are women. The prospect in some areas of the world is bleaker still. Infection in many European countries is almost on a par with that of the United States. In Central Africa, within the so called AIDS belt - over ten million people are now infected, accounting for almost one tenth of the entire population. These people also are likely to life long carriers of the disease as well.

These numbers assume even more ominous proportions when we consider the ultimate health impact of infection. We have studied this disease for almost six years. In that time we have learned to recognized the many faces of this afflication. In the early days, it was first detected by keenly observant physicians as an unusually high incidence of rare forms of cancer and unusual infections in young men. We now know that infection is manifest in many guises. Most notably, and most serious is the gross impairment of the immune system and of the brain. In its ultimate form, the disease destroys so much of the immune system that the body cannot defend itself against infection. The brain may also be reduced by massive tissue destruction to one third its normal size. Other life threatening forms of this disease include at least three types of cancer, all lethal unless treated, infiltration of the lungs with white blood cells, and failure of the clotting components of the blood.

Many of these symptoms of infection, other than the major defect in immunity, have been recognized only within the past year as being an integral part of the disease process. As much as this disease was thought to be primarily a disease of the immune system, it must now be considered to be a disease of the brain as well. Almost one half of all the people infected with the virus six years ago, have some major serious medical symptom of infection and the toll may rise still further.

The most recent studies of the fate of infected people paint a picture that is consistent with a slow progressive degeneration of the immune system and of the brain. A recent eighteen month follow up investigation of infected soldiers completed by the U.S. Army reveals a pattern of continuously worsening disease status in the majority of those infected. Those with no symptoms or mild symptoms progressed to more serious symptomatic states. Those with serious symptoms progressed to death or to terminal illness. One third of the soldiers studied in this group were women. Their disease progressed in a fashion indistinguishable from that of men. AIDS is a disease that does not discriminate on the basis of sex. The slow, perhaps inexorable progession of the disease is consistent with what we know about diseases caused by viruses similar to the AIDS virus in animals such as sheep and goats infection is followed by a degenerative process that occurs slowly over a period of years. We must be prepared to anticipate that the vast majority of those now infected will ulimately, over a period of five to ten years, develop life threatening illness. I do not need to tell you what the impact of this disease will be on a health care system. We see this wave of devastating disease approaching. The magnitude and nature of the problem is crystal clear. As the disease continues to spread, the magnitude of the problem must increase. I urge you to begin planning now for the inevitable.

How did this unwanted spector appear so rapidly? We now know that a spread of the disease in the United States and Europe was preceded by a massive spread of disease in Central Africa. As best as we can tell, the disease began about twenty years ago. By now, one tenth of the adult population of Central Africa is infected - half of them being women. We also know that a virus, very similar to the virus that causes AIDS in humans, is found in wild colonies of green monkeys inhabiting Central Africa. In the green monkey, the virus does not seem to cause serious illness, or if it does, the symptoms come on so slowly that the monkey dies of natural causes before the virus works its damage. However, as is often the case with viruses that jump the species barrier, this virus is much more damaging to the new host species, in this case humans, than to the species of origin. The virus seeks out different types of immune cells in humans as compared to monkeys. Humans also live much longer than do monkeys and for this reason what in a monkey population might be a tolerable rate of progressive brain disease is intolerable to us. As best as we can peer into the past, it appears that sometime within the past twenty to thirty years, a monkey virus crossed the species barrier into humankind. Thereafter, it has spread with alarming speed throughout the African and now the world population.

What accounts for both the rapid and widespread distribution of infection? The answer to this question lies in the nature of the disease agent itself, and its mode of transmission. In what must be regarded as a mixture of intuitive brilliance and great good fortune, the microbe responsible for this disease was isolated within three years of the first clinical description of the disease itself. That it was found at all is a tribute to the commitment that has been made to biomedical sciences over that past twenty years. The particular field of expertise from which the discovery of the virus arose, was that of cancer research, more specifically the virus cancer program of the National Cancer Institute, a program that itself was at the time of discovery of this virus well past its heyday. This program had received a burst of support in the early days of the National Cancer Program beginning in early 1970's. More recently, this program was in the process of slowly being dismantled as the promise of early production of vaccines to human cancers had not been realized. Interest in this program was rekindled prior to the discovery of the AIDS virus,as recent work originating in that program had revealed that a rare form of human leukemia was indeed caused by a virus. Work on this newly discovered leukemia virus as well as the methods developed for detection of and vaccination for the virus were underway at the time the AIDS epidemic was first noted.

Analogy played a central role in the discovery of the AIDS agent. Certain similarities including the type of cell infected, the modes of transmission of the AIDS agent, and the type of immune abnormalities present in affected individuals were reminiscent of properties of the human leukemia viruses. A guess was made that the AIDS agent might be similar to the leukemia virus. Methods and reagents that had been used to isolate the human leukemia virus were applied to the AIDS problem, both at the National Cancer Institute in the United States and at the Pasteur Institute in Paris. In both cases, these methods resulted in isolation of the same virus. That virus is now known as either LAV (the Pasteur Institute designation) or HTLV-III (the National Cancer Institute name), and is often called either HTLV-III/LAV or LAV/HTLV-III. Intensive studies of AIDS patients have unambiguously linked this virus to disease. Another link in the causal chain between disease and this virus is the observation that exposure of some monkeys to the AIDS like virus isolated from a colony of domestic rhesus monkeys reproduces within a very few weeks both the immune symptoms and the brain degeneration typical of human infection.

Regarding the discovery of the microbes that work in this disease, without the experience and materials developed over the past fifteen years in the successful quest for a human leukemia virus, progress towards finding the AIDS microbe would have been much slower. Indeed, we still might not have known the cause of this disease today. Had the AIDS epidemic appeared in the United States twenty or even ten years ago, we would not have had many of the tools that we now possess to recognize the virus and to combat it. The discovery of the AIDS virus is an example par excellence of the wisdom of our investment in fundamental biomedical research. No one could have anticipated this new disease or the importance that studies of the human leukemia virus would have in understanding this new epidemic. It was simply a bet that paid off.

We now know that the microbe responsible for the disease is a virus, and more particularly, a member of the subgroup of viruses called retroviruses. The discovery that the virus belonged to the retrovirus subfamily offered an immediate explanation for many of the puzzling features of the disease, by way of an analogy with other retro viruses.

First, and most importantly, the discovery of the virus pinpointed the infectious nature of the disease. Before the virus had been discovered theories of the origin of the disease ranged from too much sex causing the disease to theories that involved the requirement for bizarre sexual practices including the use of chemicals stimulants during sexual intercourse. Bacteria, fungi and many different viruses were proposed as causes of the disease. We now know that people who are not infected with the virus do not contract this disease. The virus and the virus has been isolated from scores and by now hundreds of people suffering from AIDS and AIDS related disorders.

Discovery of the virus eventually led to the development of the test for virus infection. Application of the discovery to development of a test was delayed for at least one year by the difficulty experimentors encountered in growing the virus. At first the virus was found to kill all the cells infected. Only tiny amounts of virus could be made to test enough samples to establish a causal link between the disease and infection.

The key breakthrough in research in the virus came when scientists working at the National Cancer Institute were able to grow the AIDS virus in large amounts, a feat that required technical brilliance as well as good fortune. Using the large amounts of virus available, a test was quickly developed. Testing of hundreds of blood samples of AIDS patients soon revealed that all patients with AIDS were infected with this virus. This test, or a close facsimile of it, is now in use worldwide to monitor the blood supply and to assist in the diagnosis of AIDS related disorders.

Testing of blood samples for evidence of virus infection quickly confirmed what many people familiar with the disease already suspected - that a carrier state existed. Evidence for virus infection was found in people who seemed otherwise to be perfectly healthy. Such people were found nonetheless to pass on the infection and the disease to others. Initial suspicion that a carrier state for AIDS existed came from careful studies of the blood donors to people who contracted AIDS after surgery. Some of the donors to those people who were apparently healthy at the time of donation later showed symptoms associated with AIDS.

It was the magnitude of the carrier population that surprised most investigators. For every case of reported AIDS in the United States, there were about one hundred or more carriers. The results of a massive blood screening program are now coming in from all over the world. In Europe and the United States the numbers are the same, there are about one hundred times as many people that are carriers of the virus for every person infected. A similar situation appears to exist in Central Africa.

The test for infection measures the response of the body to virus. It measures the production of antibodies to the virus and does not detect the virus itself. Nonetheless, recent experiments indicate that the presence of antibodies is tantamount to infection. The virus has been isolated in more than ninety percent of people who show antibody signs of infection, regardless of the health status of the person. It seems likely that once infected, a person remains infected for life. It is also possible that a person will remain a life long carrier as well. Certain blood donors are known to have transmitted the disease over a period of many years while remaining healthy themselves.

It is the prolonged carrier state that accounts for the widespread and rapid dissemination of the infection throughout the world. Most of the people who are infected do not know it. People may be infected for more than ten years before showing signs of infection. During this entire time they may transmit the virus to others. It is precisely such inapparent infections that pose the most difficult problem for disease control. Diseases that are manifest as acute and dramatic disorders are easy to track. Such diseases may be eliminated by proper isolation and quarantine of affected individuals. However, our public health system is relativly powerless to contain the disease that shows no signs of infection for many years.

The discovery that the microbe responsible for AIDS is a retrovirus offered an immediate explanation for the carrier state. Over the past twenty five years, researchers with retrovirus have become familiar with their ways. All such viruses have the ability to convert themselves into the genetic material that is the same as that of cells they infect. This is a process unique to these viruses. The process is so unusual that it is called reverse transcription, hence the name retro virus. The discovery of this unusual aspect of these viruses life cycle was rewarded with the Nobel Prize in 1974.

Reverse transcription permits these viruses to slip into cells and to remain within the cells without causing further damage. Such viruses can persist in cells, mimicking cellular genetic material, without producing any virus at all. As the cells divide, so does the genetic information of the virus. In such fashion, individual cells remain infected for a lifetime. Therefore, the notion of once infected, infected for life is substantiated. All of our experience with this broad family of retroviruses tells us that this is most likely to be the case for the AIDS agent. Indeed, our observations with infected people and with virus carriers confirm these suspicions.

The virus in its quiet state is said to be latent. For people infected with the AIDS agent, the virus does not appear to remain only quiescent. As mentioned earlier, infection if most often characterized by a slow degeneration of the immune system and of the brain. The disease progresses at different rates in different people. The progressive nature of the disease argues for reactivation of the virus from a non-replicating to replicating state. The ability to isolate virus free of cells and from cell free blood components in many carriers also indicates that the latent virus can be periodically reactivated. This reactivated virus is infecticus for other people. Hence the notion that once infected, always infectious. Although it is theoretically possible that every infected person is always a carrier, more work is needed to define this unpleasant possibility. Certainly, many people are known to be carriers for many years. The implications of the carrier state for control of the disease and for life choices that must be made by infected people are truly enormous.

Isolation of the virus and the development of a test for infection has also hastened our understanding how the disease is transmitted. Early studies of AIDS cases completed before the virus was isolated indicated that the disease was transmitted sexually and by blood and blood products. Cases of suspected transmission of AIDS from infected mother to newborn child were also recorded. The results of the blood test confirmed these suspicion and provided us with a clear picture of how the virus that causes AIDS is, and is not, passed from person to person.

The virus is transmitted by sexual intercourse between men and women and between men and other men. There are anecdotal reports of transmission from woman to woman as well. Although it was initially thought that particular forms of sexual activity, for example oral and anal sexual intercourse, were required for transmission of the virus, it is now thought that the disease can be transmitted by vaginal intercourse as well. Infections have been documented to occur during artificial insemination with contaminated semen. Studies of blood samples of U.S. soldiers show that an infected male soldier can transmit the virus to his female sexual partners and that women in turn can transmit the virus to other males. In a small study recently conducted by the U.S. Army, more than one half of the husbands of women infected with the virus before marriage were found to be infected. Other studies show that wives of infected male hemophiliacs are very likely to be infected as are the wives of those men who become infected with the virus via blood transfusion.

In retrospect it appears that the original focus on the sexual practices of homosexuals as a means of transmission of the virus was misplaced. In the homosexual population, the virus is transmitted by these sexual practices because those are the sexual practices of the homosexual community. Early suspicion that bruising, bleeding, or abrasions facilitate infection have not been proven.

That infection spreads via blood and blood products is well documented. In the majority of transfusion related AIDS cases, it has been possible to trace the source of the contaminated blood to a single donor. Likewise, infection of hemophiliacs can be traced to contaminated blood products used for their treatment.

Development of a test for AIDS virus antibodies The discovery of the AIDS virus has greatly improved the safety of the blood and blood products used for transfusion. Blood products used for the treatment of hemophiliacs are now processed so as to eliminate the possibility of infection. The additional processing appears to be entirely effective. Although this new method of treating the blood comes late for most hemophiliacs in the United States, most of whom are already infected, it should prevent infections of newly diagnosed hemophiliacs, and if applied in a worldwide basis, should prevent spread of the infection to other areas of the world that are now free of disease, particularly the Far East.

How safe is the supply of blood used for most transfusions? Certainly the blood supply is a good deal safer as a result of the universal administration of the test for AIDS virus antibodies. However, the blood supply is not entirely safe, despite the assertions recently made by some health officials. The current blood test will fail to prevent use of contaminated blood for two reasons. The test measures only antibodies to the virus, not the virus itself. Some people donating blood will be newly infected. The blood from such people will contain infectious virus but no antibodies. Based on our experience with the hepatitis B virus, (almost the same number of AIDS virus and hepatitis B virus carriers attempt to donate blood) about 2,000 cases of infection can be anticipated per year from donations of those newly infected donors. This number will increase as the number of infected carriers.

The blood test also will fail for that group of carriers who harbor infectious virus but who do not produce antibodies to the virus. This curious, and to my knowledge unprecedented disease state, is known to occur for some healthy carriers. The antibody free carrier state was first detected in a systematic series of tests of sex partners of AIDS patients. Infectious virus could be isolated in some of the apparently healthy partners, yet these people showed no signs of infection using a battery of tests for detection of antiviral antibodies. The antibody free carrier state can be manifest for at least two years. It is believed that only a small fraction of carriers fall into this category, but more studies are needed to define the scope of the problem. The size of this population will determine the risk of blood transfusion related infections. The inherent failure of the tests for antibody to the virus demands a closer examination of blood donation policies.

The current format of the blood test has the additional problem that some people who are not infected react to the test as if they were. We know this because several different types of tests have been developed. These additional tests have the advantage of being more specific than the commercial tests currently available. They rely upon detection of antibodies to specific viral proteins rather than antibody to crude mixtures of virus and cellular proteins that make up the test matrix of the commercial kit. Comparison of the results of these tests with those of the commercial tests reveals that at least one half of the people defined as possitive by the commercial tests do not, in fact, show signs of viral infection. Antibody reaction to nonvirus proteins present in the commercial test mixtures is thought to be responsible for these false positive results.

Notification of positive test results varies according to the setting of the test and according to local regulations. The anguish caused by the reporting of false positive results can be considerable. Fortunately, it is likely that new tests will greatly improve discrimination between truely and false positive results will be available within the year. Such tests will rely on highly purified fragments of the virus produced by gene splicing technology. Although such tests will reduce the number of false positive results, it is unlikely that they will significanly improve detection of the most dangerous samples entering the blood supply, those that contain virus but no antibody. Development of reliable virus detection tests is not likely to be immediately forthcoming, particularly as infected people often have very little to no detectable virus free in their blood. In these people, the virus exists in a latent form in the blood cells which can be activated upon transfusion of that blood into another infected person.

Transmission of the virus by the sharing of needles by persons who use intravenous drugs, most notably cocaine and heroin, is increasing, and is one of the most troubling aspects of the epidemic. Needle sharing is a common practice amongst drug abusers. The virus is readily transmitted by use of shared needles. The spread of the virus through the drug abuse population, estimated to be more than one million people in the United States, is occurring with extraordinary rapidity. Recent surveys show that within the Manhattan/Newark area, between sixty to eighty percent of all drug abusers are now infected with the AIDS virus. The fraction of the population infected decreases with increasing distance from a metropolitan center. Thus, in Jersey City, the rate of infection is between forty to forty-five percent and in Atlantic City, between five to fifteen percent. The rate of infection varies around the country twelve to twenty percent in Boston, fifteen percent in San Francisco, and less than five percent in Phoenix. Infection of drug abuse populations is rampant in many European cities as well.

We can expect that unless immediate and effective measures are taken, virtually all intravenous drug users in this country and around the world will be infected within the next few years. Infection of the drug abuse population has already created a major focus of new infection in our population. This population has sexual habits that differ substantially from those of the homosexual male population.

Drug abuse by prostitutes is a major route by which the AIDS virus is now entering the heterosexual population. Recent studies estimate that at least one third of prostitutes in the United States are also intravenous drug users. Studies of rates of infection in prostitute population are now under way. Preliminary evidence indicates that infection of prostitutes with the AIDS virus is wide spread in those areas of the country where infection of the drug abuse population is common. A current best guess is that the probability of encountering infected prostitute in Manhattan is between about one and five, and in Boston between one and ten and one and twenty.

A recent survey completed in West Germany also indicates an infection of the prostitute population in that country is a problem of major proportions. Nationwide, about twenty percent of all prostitutes in Germany are infected. Infection rates differ widely depending upon whether the prostitution population is registered, operating under license from the government and subject to routine health examination, or whether the population is unregistered. Infections rates in the registered population are about one percent whereas the infection rate in the unregistered population, largely drug abusers, ranges between twenty and fifty percent. In one study, more than half of the unregistered prostitutes working the area of Berlin near the train station were found to be infected.

There is accumulating evidence that infection is transmitted from prostitutes to their customers. A recent study conducted by the United States Army revealed that ~~four~~ five percent of United States soldiers reporting to venereal disease clinics in Berlin are now infected with the AIDS virus.

As infection of the drug abuse population spreads, so too will infection of the prostitutes and their customers. The consequences of such infection for the dissemination of the disease within the heterosexual community, that is, the female sexual partners of prostitutes, customers of prostitutes, and, in turn, the male sexual partners of these women, are predictable. A lethal venereal disease is now spreading through our population, all the more dangerous because infections may remain inapparent for a long time.

Can we estimate the potential spread of this disease within the sexually active population? For such estimates, we look to the incidence of certain other venereal diseases. A little known sexually transmitted disease, clamydia, provides perhaps the best model for the AIDS infection. Clamydia infections are, for the most part, inapparent. The infection can be spread by carriers who seem to be disease free. Until recently, when an easy to use test for clamydia was developed, this infection was rarely diagnosed. Widespread use of the clamydia test revealed that a startlingly high fraction (twenty to thirty percent) of college women were infected. Unless sexual practices change dramatically in this country, it seems likely that infection of our young population with the AIDS virus may reach similar high levels.

Widespread use of the antibody test has also established how the virus is not transmitted. At present there is no evidence of which I am aware that the virus can be transmitted other than by sexual contact (possibly also including exchange of large amounts of saliva), by needle, and by mothers to their unborn children. The evidence of observation on this score is substantial, but is most dramatic in studies of health care workers who treat AIDS patients. There have been in total, more than one million days of contact between AIDS patients and medical personnel including doctors, nurses and support staff. In no case has the contact between the AIDS patients and their health care workers been known to transmit the disease. The health care workers who have become infected either with the virus have been shown to contract the infection outside of the hospital either by drug abuse or homosexual activity. A few documented cases of infection of health care workers via accidental injection of AIDS patients blood are the exceptions that prove the rule.

Assurances from the medical community that the virus is hard to catch and is not known to be transmitted by either touching AIDS patients, drinking from the same glass as an AIDS patient, or being sneezed upon by an AIDS patient, or even being bitten by a juvenile AIDS patient have not been entirely effective in allaying the public's fears of contagion. Some of the difficulty public health officials have in explaining the situation to the public can be attributed to problems of language and thought patterns of the biomedical community. Scientists and physicians are rigorously taught not to speak in absolutes if there is a possibility of a doubt. The observation that the AIDS virus can be found in saliva, in tears, and in other body fluids opens the theoretical possibility that the virus may be transmitted by casual contact. That our overwhelming clinical and epidemiological experience tells us that the virus is not transmitted except via intimate sexual contact or by blood or blood products does not alter the caution that years of training has instilled to be aware of the improbable. If the same people were asked to comment on the possibility of casual transmission of syphilis or gonorrhea, the answers they would give would be very similar to those given for AIDS - Yes, it is theoretically possible - No, these diseases are not usually transmitted by casual contact. Perhaps it is the newness of the disease, the aspect of the unknown as well as the lethal character of the infections that shapes the public's concern.

This being said, people who work with the disease are puzzled by the emphasis it has now placed on restricting the activities of AIDS patients themselves as these patients represent a small minoriy of the potentially infectious population. The major risk to our entire population lies in the large number of AIDS virus carriers who are unaffected by the focus of the AIDS patients themselves.

Whatever policies are put into effect to control the spread of this disease, these policies, must to be effective, address the problem of the healthy AIDS virus carriers. Such policies must also be thought through with great care as they will surely affect upwards of one million of our fellow citizens for a lifetime.

Another mode of transmission of the virus is from mother to unborn child. The risk of infection of an unborn child born to an infected mother is extremely high, exceeding 70% in some studies. Transmission from an infected mother to a nursing child may also be possible. Infection in newborn children results in serious disease. Policies regarding counseling of infected mothers must be carefully considered.

THE TASK AHEAD

The anticipated impact of the AIDS epidemic on world health is enormous as well as frightening. What is being done and what can we do to control this disease.

Our first and present only major tool in combating this epidemic is communication. Fortunately that is one of the strongest traits of our species. Information regarding the nature of the disease, the modes of transmission, and the steps that can be taken to avoid exposure to the disease must be disseminated widely, not only in this country, but throughout the world. Details of how the virus is and is not transmitted should be known by everyone. The concept that a new lethal venereal disease is afoot must be made known to every sexually active person so that people can modify their behavior accordingly. The problem of transmission of the virus via use of shared needles by drug abusers must also be addressed, and addressed quickly if this problem is to be arrested.

Despite our best efforts of communication, I believe that the epidemic will spread. Communication will help to slow the course of this epidemic. However, the disease is transmitted by our all too well known characteristics of human sexuality and attraction for chemical relief from worldly pains. I think it unlikely that any amount of education will eliminate sexual promiscuity or drug abuse. We need only to glance back at the past when syphilis was a lethal disease. Most people knew how to avoid the disease, yet many of the most famous figures in our history, among whom were the most knowledgeable persons of their time, contracted and died of this disease. It is unlikely that we will show more restraint or greater sense than our forebearers.

The task then falls to the biomedical community to wage a successful battle against this disease. As a researcher in this field, I am often asked why hasn´t a vaccine or treatment been forthcoming. When will vaccines and treatments be available? Indeed, the progress of the viral medical science in our lifetime has been remarkable and until now have eliminated serious threat of infectious disease and epidemics in most parts of the industrialized world.

In the past 30 years we have witnessed the eradication of smallpox, development of vaccines for polio, mumps and measles and introduction of many new antibiotics and several new antiviral drugs. The rapid success of the biomedical community in identification and elimination of such newly perceived threats such as the Legionnaire´s disease has increased our faith in the ability of the biomedical community to respond quickly and effectively to new health challenges. To be sure there is a lingering current of skepticism with regard to what medicine can do. Most cancers are still untreatable. No one has yet developed a treatment for the common cold. The symptoms of Herpes virus infections can be moderated but not eliminated. Heart disease is still a major health threat. Still, this being said, most people wonder why we have not yet developed a vaccine or treatment for AIDS. Frequently one hears the question, "Isn't AIDS after all an infectious disease of the type we know how best to handle?" The failure to produce effective prevention or treatments calls into question just what has been done with research on the AIDS problem. Below, I summarize the remarkable progress that has already been made. I also highlight what remains to be done and suggest ways to approach the problem in the future. What follows amounts to a guide to what can and cannot be done with contemporary biomedicine.

Progress and understanding of the disease has been remarkable, both in the swiftness and the initial perception of the problem and the clarity of or immerging picture of the disease. The malady was first detected by observant clinicians as soon as it could have been detected in the United States given the long latent period of the appearance of the first symptoms in infected people. Awareness that a new disease was afoot can be attributed in part to the unusual nature of the symptoms, a rash of rare cancers, Kaposi's sarcomas, and unusual infections in young men, and partly to the acuity of the clinicians who encountered the disease. A description of the underlying immune defects was made within a year of the first diagnosis of unusual symptoms. Two years after the initial diagnosis, the scientific and medical literature was repleat with reasonably accurate clinical descriptions of the multiple aspects of this disease. The Centers for Disease Control in Atlanta was tracking this new disease, and keeping careful records of its progess within months of the first case reports. Studies on mechanisms of transmission were well under way within the first year. Sexual transmission, transmission by blood and blood products were quickly documented. The scientific community was placed on the lookout for the cause of the new disease. A series of scientific meetings was organized both by the National Institutes of Health, the National Cancer Institute and the Centers for Disease Control to consider and to review progress.

In retrospect, we know from studies of preserved blood samples that the very first infections occurred no earlier than 1976. Significant increase in the number of infected people within the United States did not begin until about 1978. The first cases of this disease were recognized by 1980. The latent period for this disease is typically longer than two years. The rapid recognition of this disease is testimony to the high quality of our health care delivery system. Early diagnosis and detection of the disease in the United States is in sharp contrast to the situation as it occurred in Central Africa. The first indication that the disease was present in Africa came from reports from physicians in Brussels and Paris who reported that wealthy people with full blown symptoms of AIDS were appearing in their hospitals for treatment. In late 1983, an international team of physicians traveled to Central Africa to investigate whether AIDS was present in that region. In early 1984, they reported the startling finding that within a single week they had diagnosed thirty-five new cases of AIDS at a single hospital in Kinshasa - the first thirty-five cases of AIDS ever dianosed in Africa. Evidentally, the disease had been raging in Central Africa for up to ten years before the first African diagnoses were made. To be a sure a diagosis of AIDS in a country of high infectious disease is not straightforward. People who have AIDS were evidentally diagnosed as dying from infections characteristic of weakened immunity. Nonetheless, the lesson is clear. A major new disease that now threatens the health of the entire world raged uncontrolled and unchecked in Africa for at least ten years. It is only prudent to consider the establishment of modern well equipped, well staffed scientific sentinel post in Africa to monitor future disease outbreaks, particularly as I shall argue later that AIDS is but one of a series of diseases that we can expect to spring from this continent in the future.

The scientific background of the major participants in this phase of the discovery have been remarkably similar. Almost every one of the scientists both in the United States, in France and in other countries have had years of training in the same small field of research, that is, retrovirology, the study of this subclass of viruses. Moreover, most of the key scientists involved in this work have been working with that subset of retroviruses associated with human leukemias. The payoff for this training for the solution of some of the problems regarding AIDS has been simple and direct. These scientists used methods and reagents they had developed for the study of the human leukemia virus for a study of the AIDS virus. The result is that within an eighteen month period our knowledge of the AIDS virus now equals or exceeds our knowledge to any other animan or human retroviruses.

It is also notable that almost to a person scientists in Europe and America who had been working with the human leukemia virus began to work on the AIDS virus as well. Such conversion did not, and still has not occurred to a significant extent in Japan. The continued commitment of the Japanese scientists to the human leukemia virus is all the more remarkable as Japan alone has more scientists working on the human leukemia retroviruses than all of the rest of the world combined. The most ready explanation of the difference is that the Japanese view the human leukemia virus as important for their country, a view understandable in terms of the high rate of epidemic infection of certain parts of the population with the leukemia virus. Evidentally, they do not review AIDS as a serious threat to their country, a view that seems destined to change.

The single greatest step in the understanding of the disease was the isolation of the AIDS virus and the forging of a causal link between the virus and the disease. Large amounts of virus have been available for study for eighteen months. This period has seen an explosive growth in our understanding of the virus.

In quick succession, the virus genetic material was converted into convenient forms for gene splicing and the complete genetic code of the virus deciphered in several laboratories both in the United States and in France.

To understand the magnitude of this achievement, we must compare the progress with this virus to that of other viruses. Although the polio virus, the yellow fever virus and dengue viruses have been known as human afflictions from time in immemoriam, the complete genetic information of the polio and yellow fever viruses was deciphered in only the last year, and that of dengue virus is still unknown. These viruses are smaller and more easily grown than is the AIDS virus.

In related progress, the structure of most of the constituents of the virus particles itself were uncovered. This a particularly important advance as it is our reaction to these virus components that must be exploited for the detection of the virus itself and for vaccine development. Understanding of the virus was greatly accelerated by comparison of the genetic information of the new virus to that of other well studied members of the retrovirus family. Analogy, based on years of careful investigation of these other viruses proved to be an invaluable tool in speeding research on the AIDS virus.

A clear map of what virus constituents are recognized by the body's immune system has also been developed. The initial murky reports on this aspect of infection have now been clarified. The new generations of the diagnostic tests for antibody detection will depend upon this newly won knowledge.

The past year has also witnessed remarked progress in understanding the damage wrought by the disease. A major advance has been the recognition that the brain is a primary site of infection. This realization was somewhat slow in coming, most probably because the time required for appearance of gross symptoms of brain degeneration is long. Disordered mental states and other manifestations of brain disease was earlier attributed either to depression associated with diagnosis of AIDS or to opportunistic infections of the brain. However, discovery that the AIDS virus replicates in the brain has altered this picture. The early onset of infection of the brain will surely complicate treatment of this disease, as a barrier between the brain and the blood exists. This barrier normally serves to insulate the brain from fluctuating levels of chemicals in the blood, but it also serves to exclude most drugs from the brain.

Observations of large number of infected people have been possible only recently as the numbers of infected people has been rising rapidly over the past few years. Such observations permit unusual symptoms of the virus infection to be identified. In recent months, several additional forms of cancer, Hodgkin's lymphoma and Burkitt's lymphoma have been added to the roster of virus related disorders. It is suspected that infection with the virus might also excelerate the onset of cancers of the mouth, heretofore typically associated with smokers. An unusually high occurrence of pancreatic cancer has also been noted in some patients. Two additional virus related disorders include defects in the blood clotting components and infiltration of the lungs with white cells. The latter symptom is particularly prevalent in children who have been infected.

Progress and understanding of how the virus infects cells has also been rapid. It was originally thought that the virus infected only certain types of immune cells. This specialized immune cell, the T4+ cell, is central to the proper functioning of the entire immune system. Some researchers have likened the T4+ cell to the conductor of a symphony. We know that the immune system is comprised of multiple components that interact and harmonize in an intricate way. Death of this central controlling cell, due to virus infection, it was argued would destroy the integrated functioning of the entire immune system. Although this picture remains accurate, it is now thought to represent only a partial truth. We now know that other components of the immune system are infected with this virus. Even if these other parts of the immune system are not killed outright, their proper function may be altered by virus infection. In the model of the immune symphony orchestra, not only has the conductor been murdered but the first violinist, the drummer, and the horn section are wounded as well. The full extent of damage to body tissues wrought by virus infection has yet to be assessed.

The past year has also witnessed the discovery that some people infected with the virus produce antibodies that inactivate the ability of the virus to infect new cells. Not all infected people make such antibodies, and those that do often make these antibodies in trace amounts. This observation has important implications for the development of a vaccine. Antibodies that prevent virus from infecting cells are needed for protective immunity. A successful vaccine must elicit such a protective response. The finding that humans can make such antibodies is encouraging.

However, along with encouragement comes puzzlement. Not everyone infected makes such antibodies - why not? We do not know. Many people who have such antibodies including those with the highest levels of these antibodies, still die from progressive distruction of the immune system and of the brain. Why? We do not know. Such antibodies do not protect people who are already infected. Will such antibodies protect against initial infection? The answer is not clear. Some people who are infected remain disease free for a long time. Many of these people do not have any antibodies to the virus at all. Is it possible that antibodies are part of the disease process itself and not part of the body's defense to the virus? Certainly we know that antiviral antibodies are implicated in the disease processes of several other infections.

Finally in the past year we have learned something about the special method this virus uses to propagate itself. Upon infection, the virus produces a product that alters the environment of the cells so that viral products can be made at a greatly excelerated pace. This positive feedback control is one of the reasons the virus reproduces itself so profusely. The prolific capacity for virus replication conferred upon the virus by this positive control process accounts for the ability of the virus to establish infection at many sites once it infection occurs. The precise regions of the virus that are necessary to accomplish the speeded up replication have been elucidated. Such elements, in the configuration in which they are found in the AIDS virus, have not been witnessed heretofore. The positive control process may prove to be a prototype of regulatory processes of normal cellular genes, and may provide insights regarding the functioning of the unaffected immune system.

The discovery of the positive regulatory control mechanism for virus replication has a further implication that it may provide a target for antiviral drugs. The pharmacologist always seek drugs that interfere with the virus growth but that do not interfere with the normal cellular function. Such is a difficult task as viruses use most of the cellular machinery for their own reproduction. Very few mechanisms of virus reproduction differ from normal cellular processes. The genes that positively control the replication of the AIDS virus represent one possible difference in the virus life cycle that might be exploited by the clever therapist.

The progress in understanding the virus has been rapid is evident. In surveying such progress, it is notable that with few exceptions, the progress that has been made so far is in precisely those areas in which substantial advances have already been made in other fields of virology, particularly in studies of other retroviruses. The real work of discovery regarding this virus has now just begun. The second phase of discovery promises to be much more arduous then the first. We have now progressed into the broad sea of the unknown. Our beacon of analogy is no longer in sight. We confront problems never before encountered. The solution to these problems will require great ingenuity. In some cases it is clear that even the fundamentals of the basic workings of the cells that must be understood in order to understand the disease process are not known. This is an area of enormous interest to the scientist. We are propelled into this area by a sense of urgency of the problem, we are lured into this area, by the prospect of new and uncharted vistas. We are energized by the excitement of our colleagues and by the hope of fundamental new discoveries. We are spurred to extraordinary efforts by a spirit of competition to be the first to understand the workings of new living things.

All this is wonderful news for the scientist in us. However, it is sobering and even bad news for all of us who seek a speedy solution to the problem of AIDS. All of us working in this field are certain of one thing, we know that we do not know enough to know when, or even if, effective vaccines or therapies can be developed. Given our present state of knowledge of this new virus, and its multiple interactions with the body, we know that it will take a stroke of extraordinary good fortune for us to develop either an effective vaccine or therapy. The attempts in this direction now being undertaken are equivalent to shots in the dark or at least shots in the twilight. We know how much remains for us to learn. Our progress to date can be summarized as providing little more than a map of the terrain, a preliminary ranging of the task before us.

Perhaps we shall be fortunate. I once read that intelligence is the ability to reach the correct conclusion on the basis of insufficient data. Surely, we have an insufficiency of facts. Perhaps we will be either clever enough or lucky enough to guess right in our early attempts at vaccines and therapies. After all, some of the highlights of medical history represent just such intelligent guesses. Louis Pasteur developed vaccines for rabies and for small pox before viruses were discovered. The yellow fever vaccine was developed in a unique series of experiments that have not been repeated even today. We must pursue both intuitive as well as thoroughly systematic approaches to this problem. The magnitude of the threat that this disease poses to our species demands nothing else.

A PROGRAM OF FUNDAMENTAL DISCOVERY

The scientific assault on the AIDS problem requires three simultaneous and interlocked scientific programs - a program of fundamental discovery, a program of vaccine development, and a program to develop effective treatment.

We must understand the workings of this new virus. Insofar as the AIDS virus is similar to other previously studied retroviruses, we understand it. However, in the search for the cause of the AIDS virus, a net was cast to pull in a virus that was thought to be similar to that which causes human leukemia. A very different creature was landed by this effort. Perhaps when we know much more about the AIDS virus we shall understand why fishing for a leukemia-like virus netted us this very different creature. We now find ourselves very much in the position of Columbus who set out to find a route to India by sailing west. What he found was a new continent. The AIDS virus is our new continent. To be sure, the virus shares many features in common with other retroviruses, but it also very different. Already we have discerned that this virus has at least six genes whereas most of the retroviruses we have studied have only three. There is much uncharted territory to explore with this virus. Fortunately, we have powerful tools for such work. We are confident that the major features of these new genes will be understood within the next two to three years. It is possible that the genetic information of this virus still contains more as yet undiscovered genes and encodes functions that are still hidden from us. It is our job as scientists to find out what these functions are.

We must also learn how this virus lives with and/or kills cells that it infects. Some cells apparently harbor the virus in a silent form and show no outward sign of infection. Other cells are infected and produce virus but do not die. Still other cells die as they are infected. It is possible and even likely that some cells respond to signals produced virus infected cells. Such cells may be driven to a frenzy of replication leading to formation of certain types of cancers, or on the other hand they may die in response to infection at a distant site. We know that the virus infection results in massive destruction of the brain, but we have no understanding of how or why such cell death occurs.

We must understand the body's immune reactions to these virus. It is already evident as described earlier, that the immune reactions to this virus are many and varied. That this must be so is inherent in the nature of the virus infection. This virus infects and destroys the very cells that control the immune reactions to the virus. We know too little about the complex interaction of the immune cell regulation to know just how this virus disrupts the normal function of the immune system. We know that immunity to foreign substances can be effected both by antibodies that circulate freely in our blood and by certain white blood cells. We understand something of the antibody response to the virus but we have very little understanding of the basis of cellular immunity to these viruses or even whether it occurs at all. Tools for such studies are available but they represent the very forefront of contemporary research in immunology. We have no choice but to delve into this area as this is where the pathology of the disease and our desire to create vaccines must lead us.

Each of these scientific efforts represent forays into the unknown. It will take our best intellects, working in many different disciplines - biochemistry - molecular biology - cell biology - virology - immunology - neurobiology - and pharmacology to unravel these problems. We are fortunate that this country is rich in the expertise required for understanding of these problems, the result of years of far sighted support of fundamental science.

Despite the need for and excitement of AIDS research, the biomedical community both within the United States and abroad, with some few notable exceptions, has remained curiously inert, seemingly immersed in their ongoing projects. We have not yet seen a major reorientation by many of our best researchers to study the problem of AIDS.

The one notable exception to this overall picture of scientific mention in the United States has been certain government laboratories both at the National Cancer Institute, the National Institutes of Allergy and Infectious Disease. A great majority of research in this country has been done at the National Cancer Institute mostly because the requisite expertise for the study of retroviruses was there. Some commerial companies have also entered the field of AIDS research, but for the most part these efforts have remained focused on narrow commercial objectives. We cannot rely upon the "product" oriented laboratories of commercial houses for solutions of the fundamental scientific problems. Although there are some signs of change in this biomedical community, it is safe to say that with the exception of these government laboratories, that very few first rate scientists in our research institutes and academic laboratories have turned their attention toward the problem of AIDS. The progress that has been made is all the more remarkable for the limited number of scientists engaged with this problem.

Why the curious inertia? For scientists, as for everyone, AIDS is a disease we did not need. Our lives, careers, laboratories are full to bursting. This is the golden age of biological discovery. A talented biologist finds pure gold around every corner and under every stone. Every first rate scientist has more exciting projects under way than can be easily managed. They are already stretched to the limit, full of their own possibilities. For our best scientists to work on AIDS must needs mean that other exciting work must be neglected.

Scarcity of funding is another reason our best scientists have been reluctant to enter this arena. The broad base of support for the biomedical research has been perceived by most scientist to be eroding in recent years. We are fresh from the recent devastating attacks of the Office of Management and Budget that sought this year to reduce by one quarter the total number of research grants in biomedicine. The total number of these grants was only partially restored after a long debilitating and bruising battle with the executive branch. Funding in biomedicine is now seen to be uncertain. Our very best scientists have had grants rejected for the first time in many years. In this climate, those scientists think it best to stick to those areas in which they have a proven track record. It is viewed as dangerous and unwise to move into what might be new and difficult scientific turf.

There exists more specific funding problems for the AIDS research as well. Despite the assertion by the Administration that AIDS is the number one health problem priority in the United States, support for AIDS research has been woefully inadequate, with the notable exceptions for epidemiological studies at the Centers for Disease Control. The Administration claims to be spending niney-six million dollars this year on AIDS research and proposes to spend one hundred and twenty six million dollars in the coming financial year, 1986. This would seem to a lot of money, but closer inspection of these figures reveals that a good deal of what is called AIDS research money is really the same money given to these institutions as before AIDS was ever recognized as a problem. The exception to this has been a greatly increased funding of projects at the Centers for Disease Control. Even this year, the proposed budget is not achieved by addition of new money to the budget, but rather by shuffling of already allocated monies. In some cases, paricularly for the National Cancer Institute, this new money is nothing more than taking the money from one pocket and putting it into another, a choice the Director of the National Cancer Institute is free to make on his own.

Budget debates as to how much is enough are endless. What is clear is the message as perceived by the scientific community. This message is that there is a lot of talk about AIDS but no new money significant for AIDS research. Grants on this subject are handled very much on a business-as-usual basis. They are reviewed for scientific merit in a leisurely process. Grants that propose specific programs targeted for AIDS therapy of vaccine are often rejected as not relevant to biology in general. No one can fault the review committees who rejected such grants, as they have been asked only to judge programs based upon their scientific merit and not upon their relevance to a health issue.

This is today's reality. Adequate funds are simply not available to attract the best minds in our country to the problem of AIDS. As the solution to the AIDS problem is likely to require innovative, multidisciplinary approaches, the current situation is intolerable. We have the best biomedical apparatus in the world. Much of it is lying idle with respect to the AIDS problem as a result of inadequate funding and short sited programatic efforts. A further note of caution to the AIDS effort is that once a decision to enlist our best scientists outside the government has been taken, a great deal of care must be exercised in how this community is mobilized. The independence and creativity of these scientists is their strongest asset. The science of AIDS research now needs creativity, an ephemeral quality. There is a danger that when funds are finally made available they will be for only narrow preconceived research programs,

This is very much the character of most requests for research proposals today;

Although such vehicles are appropriate for some specific purposes, they are not well suited to the recruitment of creative talent. It is unlikely that such narrowly based programs will lead to the solutions of the fundamental problems that we now face . Nor is the establishment of a central coordinating office for all of AIDS research necessarily that which is most needed for fundamental research. Over-administration will discourage the most creative scientists from entering the field, feeling as they must, that they cannot relinquish the direction of their own research to others. We need such scientists to be creative in the mode best suited to their own idiosyncratic natures.

NEW VACCINE DEVELOPMENT PROGRAM

As acute as is the need is for mobilization of our best scientists to work on fundamental aspects of the AIDS problem, so too is the need for a major vaccine development program.

The problem of vaccine development promises to be a difficult for several reasons. The nature of the infection itself poses the most fundamental difficulties. Once a virus enters a cell, it may lie dormant, hidden from the immune system. Moreover, even in an active state, viruses may be transferred from cell to cell by direct contact between cells. It may not be necessary for the virus to leave the protective environment of the cell in order to spread. Cell to cell spread of the virus may be part of the explanation of why the disease progresses in the presence of good antibody responses to the virus in some patients. The requirement for a successful vaccine may well be that it prevents even the first round of infection from occurring - a far more difficult prospect than raising immunity against the polio virus for example, a virus that must leave the cell in order to infect new cells, and which is subject to inactivation by antibodies that can act only outside of the cell.

A second troubling feature of the virus is the extraordinary speed at which changes in the genetic composition of the virus occur. The AIDS virus may change so rapidly that it can outpace the body's immune response. The extent to which virus variation represents difficulties for vaccine development is as yet unknown but the pace of virus change is clear. This virus changes its structure at a rate that is perhaps one hundred times faster than the troublesome influenza virus. An additional potential difficulty is the possibility that the immune response to the virus infection might be part of the disease. It might prove to be very difficult to sort out what types of immunity are likely to be beneficial rather than harmful. There is indication that some types of immunity may accelerate onset of symptoms once a real infection occurs.

From the above, it is evident that a well conceived innovative of vaccine development is required. At present we have no such program. Our current efforts are neither well coordinated nor well funded. The major effort in this country, private firms excepted, is directed by the National Cancer Institute. This program exists only because a small committed group of scientists will it to exist. No infusion of new funds has been provided to this or any other vaccine development program. The current budget for financial year 1986, submitted by the Secretary of Health, poses a mere $150,000 additional funds for investigation of the properties of the exterior components of the AIDS viruses, thought to be the key components necessary for the development of a successful vaccine. This amount is less than that required for work on this problem by one single laboratory. This request is a functional equivalent of ignoring the problem entirely. The proposed budget or FY ´86 is similarly meager with respect for testing vaccine preparations for efficacy and safety.

The need for large well organized, well funded programs for vaccine development is clear. Components for such programs include.

- Fundamental investigation of antibodies and cellular immune responses to virus, virus components, and virus infected cells. This enterprise should and could involve many laboratories.

- Purification of large quantities of virus components to be made available to interested investigators.

- Development of reagents for potential use as vaccines, including killed virus preparations, live attenuated virus preparations, preparation of subviral components that are inert, preparations of live carrier viruses that contains inserts of key components of the AIDS virus genetic information. There are many different appproaches to the development of successful vaccine preparations. Many of these approaches have been available only recently due to gene application of gene splicing methods. Many laboratories should be involved in attempts to design effective vaccine preparations.

- Development of a good challenge system. The efficacy of a vaccine must be tested in animals. For this purpose it is necessary to develop a model for infection by this virus. This part of the program itself constitutes a major stumbling block. Animals susceptible to the virus must be found. The biology of the virus infection in these animals must be developed. Sensitive measures of the animals immune response to the vaccine and to virus infection must also be developed. In this way, and only in this way, can the ability of vaccine preparations to protect animals be evaluated.

- Shortly we may be in a position with AIDS virus vaccine preparations of having many things to test but no systems in which to test them. This is an unusual situation for work on any virus, as for most viruses, the test systems have been developed by years of experimentation with animal models. we are in this position because the AIDS virus has been isolated only recently. Even if a good vaccine preparation were made today, we would not know it, as we have no system in which to test it.

- Development of a monkey model. The discovery that the rhesus monkey virus, and perhaps the African green monkey virus, induces an AIDS like disease in certain other monkey species in a short period of time provides an opportunity for testing prototype vaccines.

The vaccine development program as outlined above, in contrast to the program for fundamental discovery, requires a well developed, well coordinated structure as well as substantial funding. Expertise in such program is available both within the National Institutes of Health and the National Cancer Institute. The ongoing programs for vaccine development are woefully underfunded. Vaccine programs mounted at present are of necessity narrow in focus and for that reason are very likely to miss the mark.

A PROGRAM FOR THERAPY

The need for a well coordinated, well funded approach to therapy was underscored by recent congressional testimony on the subject. Witnesses for the hearing at the House of Representatives were unianimous in their recommendations for the establishment of a nationwide program of clinical trials for agents that might be effective in the treatment of AIDS.

The situation in the United States regarding trials of new anti-AIDS drugs was highlighted recently by Mr. Hudson's much publicized trip to Paris to seek treatment for AIDS. His situation was no different from that of other Americans. There is no nationwide program to develop successful therapy for AIDS. Such programs as do exist are investigator initiated, are small, and are not designed optimally for yielding of data which is be useful for systematic development of successful therapies.

The difficulties in treating any virus disease are well known. Until recently chicken soup and bed rest were the recommended therapies for all virus infections. Treatment of AIDS virus infections may be especially difficult, particularly as these viruses infect the brain early in the disease process.

For the AIDS virus, the current therapeutic strategies involve limiting the spread of virus infection within the infected person. This might be done by inhibiting early stages of virus infection. Drugs directed toward inhibition of the positive control mechanism were discussed earlier. Another and more frequently discussed target for antiviral drugs is the reverse transcriptase. Reverse transciption using a unique viral enzyme is part of the early stages of viral infection. Drugs that inhibit this part of the virus life cycle might stop the spread of the virus but spare cells from toxic effects of treatment.

Whatever therapy is developed, it is likely that treatment will be administered life long. It is extremely unlikely that all of the virus can be eliminated from the body particularly from centers of infection wherein it lies dormant for a time. Life long therapy necessarily requires that the drugs be well tolerated and have minimum side effects. Successful drugs must also cross the blood brain barrier. Administration of these anti-viral drugs must be compatible with treatment programs for acute aspects of AIDS related illnesses. These are tough requirements for any treatment program. The requirements for AIDS treatment resemble in many respects the strategies needed for the development of new cancer therapies. We are fortunate that over the years we have created a splendid apparatus for implementation of such clinical trials, This apparatus functions smoothly for contemporary programs of cancer treatment. Such programs involve coordinated efforts to develop drugs, to investigate the toxicology, the pharmacology and the animal toxicity of the drugs, to assess the impact of these drugs on selected patient populations, and to extend small scale trials to large scale clinical investigation , . These efforts involve cancer treatment centers across the country and around the world. Large statistically significant patient populations are entered into specific clinical trials that are evaluated by teams of biostatisticians.

The necessary expertise and experience for design and execution of these trials exist today. It takes but the desire and the funding to turn this apparatus toward the therapy of AIDS.

Development of therapeutic programs are expensive, for in addition to research they require patient care. Once such programs are established, caution must be exercised to assure that the trials of new drugs do not consume all of the available AIDS research funds. The needs of therapy always appear to be immediate because patients are dying. However, the needs of fundamental research and for vaccine development are equally important as it is only through these efforts that the disease can be prevented and ultimately cured.

Progress in development of effective AIDS therapies might also represent progress toward chemical prophylaxis. Drugs that stop virus from producing once infection has been established might also prevent infection ab initio . Such drugs in combination with vaccine preparations might be particularly effective.

An extremely large market beckons successful manufactures of such drugs. A patient population numbering several millions will require daily adminstration of these drugs. An even larger population is likely to be interested in chemical prophylaxis. Given this opportunity, it is surprising that most major pharmaceutical firms appear to be inactive in this area of pharmacology.

The overall picture that emerges regarding AIDS research is disquieting. It is an image of growing concern but little action. What progress has been made to date should not provide comfort that we can with a similar level of effort solve the problem of AIDS. It is most likely that given our current level of effort this problem will be solved soon, no matter how brilliant or industrious the scientists work in this area might be. We cannot even be sure that given a major commitment and mobilization of much of the biomedical research resources , a vaccine or therapy will be forthcoming in the near future.

Why such inaction in view of the mounting disaster? Part of the answer probably lies in the facts that AIDS was first evident as a major problem in the homosexual population. It is also a venereal disease and one contracted by drug users. As such, there is a repugnance felt by many parts of our society for this disease. I believe that the problem in approaching this disease lies deeper still. No one likes bads news. The worse the news is, the less we like it. The AIDS epidemic is the worst of news. Our first reaction is to deny the reality of the problem. We who work with this disease daily must still remind ourselves that this disease is for real. The palpable human suffering as well as the cold logic of the numbers of affected people that we see growing daily prevent us from forgetting that this is a disease that demands our attention. But not everyone lives with this reality. So many bad things happen in our lives - airplanes crash, bombs explode, earthquakes destroy cities, friends die of cancer. Most people simply do not want to think about yet another piece of bad news. But AIDS is a problem that will not go away. Everytime that we look at it, it looms larger so that now the shadow of this disease has begun to darken all our lives.

It is also the natural human response to hope that we ourselves will be spared from this disease. We can tell ourselves that the disease happens to others but may not happen to us. Albert Camus provided a searing description of the mentality in the plague. At first people thought the disease was only a problem for rats, then for the dirty people who lived across town. The fear came home when death visited someone next door. What many interpret as homophobia regarding the AIDS problem may be that, but also at work is a desire to define any group as "them" not us. It is becoming increasingly harder to define those with AIDS as "them". "Them" now includes not only Africans, not only homosexuals, not only Haitians, not only drug abusers, not only hemophiliacs, but also soldiers and Johns or Johns' wives. I am confident that we will awake to realize what problem is in our midst, but when? And how late in the day will it be?

And always we may ask the age old question , why are we visited with this pestilence? One answer offers itself as we look back into the origin of our species, an answer anticipated by William McNeil is his classic work of the effect of disease on our species and our history, "Plagues and Peoples". It is thought that mankind evolved over a period of several million years in Africa. Along with our species evolved our parasites, parasites that are adapted not only to us but to our primate relatives. Much of humankind has now left its historic home in the wet tropics of Africa. In our migrations, we have separated ourselves not only from our ancestral parasites, that remain for the most part bound irrevocably to the tropics, but also from our primate cousins. These parasites still flourish in the rich brew of tropical climate and primate speciation. We who have been separated from these parasites for tens of thousands of years are no longer resistant to the ravages of the diseases they may cause.

Such has been the case for thousands of years. Recently the shape of the world has altered. Dakar in West Africa is now a six hour plane ride from New York City. We are once again knit to our African heritage, once again in touch with those parasites that evolved with us, parasites that are still present in the primates of Africa. We peoples who have separated from Africa are now in a position of the American Indians when they first encountered the Europeans. We are no longer resistant to diseases widespread in the old world. To compound this problem, the African continent is itself in turmoil. The past forty years have seen massive population migrations to urban centers, rerouting of waterways, and in some cases deterioration of health care systems as the result of political upheaval. The health status of many parts of Africa appears to be worse now then it was before World War II.

From this perspective, it is no coincidence that this latest scourge is of African origin. I count four major diseases that have emerged over the past 25 years from Africa; Marburg agent, assa Valley Fever, Ebola Fever and now AIDS. This pattern of thought is not new to us who have been working with the human leukemia retroviruses. Here we see evidence for that these leukemia viruses emerged from Africa along with the slave trade and European exploration. The lesson of African origins is one we should all heed. It reminds us in the words of John Dunn that "No man is an island entire unto himself." These diseases remind us that the definition of others as "them" is folly. This may be the worst epidemic to emerge from our ancestral past for many generations, but it is unlikely, given current conditions worldwide, that it will be the last one. AIDS and the epidemics to come demand our full attention.

The HTLV III Epidemic: An Appraisal

A new lethal epidemic of HTLV-III infection is rapidly spreading throughout the United States and the rest of the industrialized world. The epidemic is well established in Central Africa as well. The magnitude and nature of the problem is summarized here.

HOW BIG IS THE PROBLEM ?

More than one million Americans are now infected with HTLV-III virus. The virus was virtually unknown in the United States prior to 1978. Official estimates are that one in ten Americans will be infected with the virus in the foreseeable future.

WHAT ARE THE CONSEQUENSES OF INFECTION BY THE VIRUS ?

Infection by the HTLV-III virus is highly lethal. New studies reveal that symptoms associated with virus infection include:

1. Destruction of the immune system (AIDS), a fatal result of the infection.

2. Destruction of the brain by virus infection. Serious motor, neurologic, and psychiatric consequences are the result of direct infection of the brain by the virus.

3. Destruction of lung tissue (occurs mostly in children). This manifestation of virus infection is called lymphoid interstitial pneumonitis (LIP).

4. Predisposition to at least three types of cancer, Kaposi sarcoma, B-cell lymphoma, Hodgkin's lymphoma.

5. Persistently swollen glands (ARC).

HOW MANY PEOPLE INFECTED BY THE VIRUS WILL BECOME SERIOUSLY ILL ?

Originally it was thought only a small fraction of those infected would become ill. It is now thought that a sizeable fraction (more than 50%) of those infected will become ill with one or more of the symptoms (AIDS, ARC, LIP, brain disease, cancer). Once infected, a person probably remains infected for life. The incubation time for serious disease is measured in years. One half of the people infected six or seven years ago are now ill. The long term survival rate, 10 years or more, is unknown but may be very low.

HOW IS THE VIRUS TRANSMITTED ?

Transmission occurs either sexually or by needle. The virus can be sexually transmitted from man to women, man to man, and women to men. The virus can be transmitted by use of shared needles by intravenous drug users, and by blood and blood products via tranfusions. The virus can be transmitted by semen or by organ donors. The virus can be transmitted from mother to unborn child. The virus is only transmitted by intimate contact and cannot be transmitted by casual contact or by routine patient care. The virus is not transmitted in laboratory settings as no infections of laboratory workers are known.

CAN THE VIRUS BE TRANSMITTED BY KISSING OR OTHER CASUAL CONTACT WITH INFECTED CARRIERS ?

It is thought that the risks of catching the HTLV-III virus by casual contact are very small. It is unlikely kissing without exchange of saliva would transmit the virus.

WHY HAS THE VIRUS SPREAD SO RAPIDLY ?

It appears that most if not all people infected by the virus are carriers of the virus. People can appear to be entirely healthy yet transmit the virus. Infected people are carriers for at least one to two years before they become ill. The vast majority of poeple who spread the infection throughout the population are healthy carriers.

IS THERE NATURAL IMMUNITY TO THE VIRUS ?

As far as it is known no one is naturally immune to the virus. It is thought that men, women and children are all susceptible to infection if exposed, regardless of sexual preference, age or race.

IS HTLV III INFECTION LIMITED TO MALE HOMOSEXUALS, DRUG ABUSERS, AND BLOOD TRANSFUSION RECIPIENTS ?

HTLV III must be considered to be a venereal disease and a disease spread via the use of intravenous drugs. As such, the heterosexual population is at risk. The high prevalence of HTLV III infection in homosexuals is now attributed to exceptional promiscuity by certain segments of the population rather than unusual sexual practices. It is anticipated that the young heterosexual population ages 18-30 will constitute the next high risk group, as venereal disease commonly spreads most rapidly in this population.

In Africa infection is most prevalent in young, heterosexual adults. Promiscuity is the dominant risk factor in this population.

CAN THE VIRUS BE DETECTED ?

The current diagnostic tests measure the body's reaction to the virus (antibodies), not the virus itself. In most cases this test detects the presence of the virus. However, some people who harbor transmissible virus have no antibodies and cannot be detected by the current diagnostic test. Such people can transmit the disease in blood transfusions. No reliable tests currently exist for the detection of the virus itself.

IS THE BLOOD SUPPLY SAFE ?

The current test will detect most but not all contaminated blood. The test will probably not pick up contaminated blood from people in the early stages of infection or from those who are infected but have no antibodies to the virus. A minimum estimate is that there will be 2,000 cases per year of blood transfusion related HTLV III infections in blood screened with an antibody detection test. The statement with the popular press that the current blood test is 99.8% accurate is misleading as it fails to account for "false negatives" as well as "false positives." A better screening test is needed.

IS THERE AN HTLV-III VACCINE ?

No vaccine for the virus exists.

IS THERE A CURE FOR HTLV-III INFECTION ?

No effective treatment for HTLV-III infection exists. Certain symptoms of the disease can be treated. Such treatment includes antibiotic treatment or antitumor treatment. These treatments do not cure the HTLV-III infection itself.

IS HTLV-III A WORLD WIDE PROBLEM ?

HTLV-III infection and related diseases are reported from the western European countries and in Australia. The disease patterns of these countries is similar to that seen in the United States. The number of infected people is expected to double every year. Central Africa is a major focus of HTLV-III infection. More than one out of every 20 people are now infected with the virus in some parts of Africa.

IS THIS A NEW DISEASE ?

HTLV-III infections were unknown in the United States before 1978. No HTLV-III related diseases, AIDS, or brain disease were known before 1978 anywhere in the world.

WHAT IS THE ORIGIN OF THE INFECTION ?

It is now thought likely that the virus originated in Central Africa. Central Africa is the most heavily infected region of the world. A virus from Central Africa. It is possible that a monkey virus has entered the human population only recently.

WHAT DO WE KNOW ABOUT THE DISEASE ?

Upon exposure, the virus infects cells of the immune system and the brain. The virus then enters a latent or quiet period. During the latent period very little virus can be found in the body. However, the virus can be transmitted by infected healthy people during the latent period - the so called "carrier state". During the latent state, the virus spreads slowly either through the immune system or the brain. The details of how the virus kills immune cells and brain cells is not fully understood.

WHAT DO WE KNOW ABOUT THE VIRUS ?

HTLV-III is a new virus infecting the population. It belongs to a family of viruses called retroviruses. The genetic blueprint of the HTLV-III virus has recently been determined. This study shows that the virus is different from other viruses studied to date. HTLV-III most closely resembles viruses that cause brain disease in sheep and goats. Fundamental questions regarding the biology of this new type of virus such as how it kills cells are not fully understood. The function of all the genes, how the virus spreads from cell to cell and how the body protects itself from this virus remains to be answered.

HOW LONG WILL IT BE BEFORE THERE IS A VACCINE ?

No one knows yet if a vaccine can be made for the HTLV-III virus, or if one can be made when it would be available. This uncertainty reflects a lack of understanding of the virus and its interaction with the body as well as the lack of understanding of the disease process itself. However, we are fortunate that as a result of gene splicing and other recent advances in biomedicine a number of approaches to vaccine development are now possible.

WHAT ARE THE PROBLEMS THAT FACE VACCINE DEVELOPMENT ?

There are two major problems that must be overcome to develop the vaccine.

1. The problem of virus variation. The HTLV-III virus genetic structure changes at a very rapid pace. This rapid change poses a serious difficulty to development of a single vaccine for all HTLV-III strains.

2. The problem of surface immunity. The virus usually enters the body via the surface membranes. The type of immunity required for such infection is difficult to obtain using most vaccine procedures. Despite these potential problems, vaccine development must be a central goal of research efforts.

HOW LONG WILL IT BE BEFORE A TREATMENT FOR THE HTLV-III INFECTION IS DEVELOPED ?

No one can predict how long it will take to develop a treatment for HTLV-III. The current strategy for development of AIDS treatment is three-fold.

1. Develop drugs that stop the spread of the virus from cell to cell. Such drugs may halt the course of the disease in individuals, and reduce the chance of spread of the virus from person to person. It is likely that it will be necessary to administer such drugs on a life-long basis as once infected the virus cannot be eliminated from the body. It is possible that drugs that prevent virus replication may be used prophylactically.

2. Restoration of the immune function. For those patients with immune defects, attempts must be made to restore the immune function once virus replication is stopped.

3. Treatment and symptoms of the infection, i.e. cancer treatments, antibiotic treatments, etc.

WHAT ARE DIFFICULTIES FOR THE DEVELOPMENT OF AN EFFECTIVE TREATMENT ?

Virus infections are very difficult to treat because the process of virus growth is very similar to that of normal cells. Indeed, the virus uses the cell machinery to grow. The drugs must be carefully chosen to stop the virus from growing without affecting cell growth. There are several theoretical possibilities for drugs that may inhibit virus infections. Trials are currently underway.

Summary

Infections in the highly lethal HTLV-III virus has now reached epidemic proportions world wide. One million Americans are now infected and it is likely that more than 50% of those infected will become seriously ill within the next five to ten years. Most, but not all infections can be diagnosed by a simple blood test. No vaccine or therapy is currently available. Fundamental features of the virus and its pathology remain to be discovered. It is estimated that more than 1 in 10 Americans may be infected by this virus in the foreseeable future.

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MYTHS ABOUT AIDS

MYTH : AIDS is a disease of homosexual men.

REPLY :

AIDS is a disease caused by a virus. Anyone who comes into contact with the virus can be infected. Infections occur during sexual intercourse, deep kissing and by needle. The virus can also be acquired by infants from mother's milk and by infection while they are still in the uterus. The virus is as readily transmitted from men to women as it is from men to other men. Women can, and have, transmitted the virus to men. Everyone appears to be susceptible to the virus. The virus is transmitted venereally from prostitutes to their customers.

MYTH : Unusual sexual practices amongst homosexuals are necessary to spread the AIDS virus.

REPLY :

No unusual sexual practices are required to spread the virus. The virus can be transmitted from men to women in the course of normal sexual intercourse. Anal intercourse is not required for infection. For example, women have been accidentally infected by contaminated semen by artificial insemination.

No bruising or tears in the mucus membranes appear to be necessary for virus infection. Direct blood to blood contact is unnecessary for infection.

MYTH : It is possible to catch the virus by casual exposure.

REPLY :

There is no evidence that the virus can be transmitted by casual contact. Hospital workers who treat AIDS patients daily do not become infected. There are no known reports of people who have been infected by casual contact. As far as is known, infection requires intimate contact. However, it can not be entirely ruled out under some unusual circumstances; but if it does occur, such events must be extremely rare. There have been more than one million total days of contact between AIDS patients and health care workers. So far, not a single health care worker who did not accidently inject himself with contaminated blood has been infected by patient contact.

MYTH : Only a small fraction of people infected with the virus will become sick.

REPLY :

Current estimates are that a substantial fraction of those infected will eventually contract some serious illness. The disease has only been studied for seven years in the United States. During that time, a substantial fraction of those people infected seven years ago are now sick. It is estimated that over a ten year period, approximately half of the people who were exposed may contract some serious symptom of the virus infection. The ultimate impact of virus infection or any health status of infected people is unknown, but may be very severe.

MYTH : Circumstances other than virus infection are needed in order for the disease to be apparent. Risk factors other than the virus, including many sexual partners, infection with other viruses, exposure to unusual environmental stress, or unusual diets, must be present before an infected person contracts the disease.

REPLY :

Exposure and infection with the virus are thought to be all that is required for the disease. Evidence that the virus alone is enough comes from studies of patients infected under unusual circumstances, such as blood transfusion cases, wives of hemophiliacs, children of infected mothers. None of these people have risk factors that are usually associated with the disease. Association of the disease with a large number of sexual partners seems to reflects an increase in the chance that people who have many sexual partners will encounter someone who is already infected.

MYTH : The virus only causes AIDS.

REPLY :

The virus that causes AIDS can also cause many different symptoms. These symptoms include:

1) Destruction of the immune system, the acquired immune deficiency syndrome (AIDS).
2) Brain degeneration. The virus directly infects the brain and can cause a progressive destruction of the brain that is evident as confused mental states and problems in muscular coordination. AIDS symptoms are often misdiagnosed as either psychosis or neurological disease of some other type for example, multiple sclerosis.

3) A disease of the lung. The lungs of some people infected with the virus sometimes become filled with white blood cells. This is a disease called lymphoid interstitial pneumonitis (LIP) and especially common in young children.

4) A disease of the blood clotting components of the blood. This is a symptom known as thrombocytopenia purpera (TP). This symptom is attributed to the attack by the virus on certain cells in the blood that are required to make clotting substances.

5) Swollen lymph glands. This symptom is often one of the first signs of infection with a virus and this symptom is characterized by persistently swollen lymph nodes. This symptom is called lymph adenopathy (LAP).

6) At least three kinds of cancer are known to be caused by this virus. These include Kaposi sarcoma, Hodgkin's lymphoma, and Burkitt's lymphoma. However, it should be stressed that virus is not always responsible for these diseases. A diagnosis of Hodgkin's lymphoma, Burkitt's lymphoma, or Kaposi sarcoma does not necessarily mean that a person is infected with the virus that causes AIDS.

MYTH : The disease, like other diseases in the past, will burn itself out naturally.

REPLY :

It is unlikely that this disease will burn itself out soon. Once infected, a person is probably infected for life. Moreover, infected people are probably capable of transmitting the virus for the rest of their lives, regardless of whether or not they contract symptoms of the disease. This is the so called carrier state.

Over the seven years the virus has been followed, there is no sign that the symptoms of infection are becoming less apparent. On the contrary, the time between infection and appearance of disease may be shortening.

MYTH : In the United States, infection with the AIDS virus is restricted to homosexual men.

REPLY :

At present, there are 150,000 heterosexual people infected representing 0.03% of our population infected with the virus. Half of these heterosexuals have no known risk factors associated with the disease including homosexuality, use of intravenous drug, or membership in any of the ethnic groups which are known to be infected with these viruses. Half of the 150,000 people infected are women. This is comparable to the total number of homosexuals infected with the virus in 1980.

In other countries such as Central Africa, there are more women than men infected with the virus. In some cities in Africa, 1 out of 10 women are now infected with the virus.

It is estimated that 1,000 to 2,000 new cases of infection with the AIDS virus occur everyday in the United States. Of these, there is a minimum of 20 to 30 women infected daily.

MYTH : This will never be a big problem for most people in the United States.

REPLY :

This is a problem that could affect a large segment of the population. This will include virtually all intravenous drug abusers, most prostitutes, all hemophiliacs and a very large fraction of the male homosexual population. The virus is likely to spread next into the young heterosexual population by infection of young women. However, eventually it is likely to spread to the heterosexual male population as well. The single most dominant risk factor is expected to be the number of sexual partners.

MYTH : The French have a good treatment for AIDS.

REPLY :

No one has an effective treatment for this disease as yet. The French drug HPA 23 is not effective for the treatment of AIDS.

MYTH : The United States has an effective treatment for AIDS but it is not licensed for use.

REPLY :

There is no known effective treatment for AIDS either in the United States or elsewhere.

MYTH : There will be a vaccine or therapy for this infection soon.

REPLY :

At present no one can predict when there will be either an effective vaccine or therapy. All that scientists know now is that they do not know when either a vaccine or a therapy will be available.

THE HTLV-III EPIDEMIC: A BATTLE PLAN

A PROGRAM TO COMBAT THE HTLV-III EPIDEMIC

A highly lethal epidemic of HTLV-III infection is spreading rapidly through the population of the United States. More than one million Americans are now infected and the number is expected to double every year. Infections are highly lethal. Over one half of those infected contract serious illness including loss of immunity, (AIDS), brain disease, cancer or lung disease.

A well organized, well funded plan to combat this epidemic is urgently needed. Whereas the recent proposal by Secretary Heckler to increase funding in this area adequately addresses some of the needs, the plan is gravely deficient in several critical areas, including the urgent need for additional funding of fundamental research, vaccine development, and therapy. There is also an immediate need for reorganization and co-ordination of resources. A program to address these issues is presented below.

Funding

Secretary Heckler's program calls for a total budget of about $126 million for Fy'86 an increase $23 million from the $103 million estimated for Fy'85. For Fy'86 the Centers for Disease control are to receive $45.6 million, National Institutes of Health, $70.6 million, and the Food and Drug Administration, $6.6 million. Small amounts are to go to other governmental agencies.

This level of funding is adequate to address issues of epidemiology. The proposed Fy'86 funding is inadequate in areas of fundamental research, vaccine development and therapy.

Specific Additional Requirements Are Summarized Below:

A program of discovery - $30 million additional.

At present we know too little about the disease itself to develop effective vaccines or treatments. Current efforts are only slightly better than shots-in-the-dark. The superb biomedical community of the United States must be organized for this task. Federal laboratories of the National Institutes of Health, the National Cancer Institute, have done and are doing an excellent job. However, the job ahead is simply too big and the areas of our ignorance too great for these laboratories to handle the problem alone. A program designed to attract the best biomedical researchers in the United States to do fundamental research on HTLV-III and associated diseases should be implemented. This program can best be administered by the National Cancer Institute working jointly with the National Institute of Allergy and Infectious diseases as the requested expertise in retrovirology, immunology, drug development, patient care, vaccine development is there.

The Secretary's proposed budget includes no new funds for such fundamental research work. Only $1.4 million can be identified under the heading Diagnostic and Therapeutic agents.

It is estimated that a new program of $30 million a year for funding fundamental research on HTLV-III and disease consequences would address this need. These funds should be directed to non-governmental laboratories and should be quickly (6 weeks) reviewed and released.

A Vaccine Development Program - $30 million additional

Thanks to gene splicing methods and other recent biomedical advances, many different avenues of approach to developing a vaccine are possible. No one can predict from our current knowledge which if any of these approaches will work. Therefore, many different avenues must be explored. Testing the vaccines in animals and in monkeys must be done. Such a program requires a nationally coordinated research program of intra-governmental and non-governmental laboratories. An inter-agency task force for vaccine development with adequate funding for potential promotion of vaccine studies within government laboratories and in non-government laboratories should be devised. It is estimated a new program of $30,000,000 is a minimum required.

The Secretary's budget proposed an increase of $1 million for testing candidate vaccines in humans and $0.15 million for vaccine development. The latter request is not sufficient to fund the efforts of even one small laboratory in this area.

A Program for Therapy - $50 million additional

Cure of HTLV-III infections will require a well-coordinated, mutli-disciplinary program of research, development, and clinical trials. Models for such a program are those that now exist for development for cancer treatment. Parallels between HTLV-III infection and cancer are striking. Once infected, a person is infected for life. Therefore, treatment must be of long term duration, possibly life long. An effective program to search for a cure would include the following elements:

1. Drug development
2. Drug testing in animals
3. Drug testing in monkeys
4. Tests of the toxicology of the drug in humans
5. Implementation of clinical trials in patients on a nationwide basis

Clinical trials require a nationwide, multi-disciplinary program. Without large scale, well controlled randomized clinical trials it is unlikely that a cure for this disease will ever be developed. It is estimated that a new program of initial funding of $50,000,000 for the first year, to be accelerated according to the success of the program, would be required.

The Secretary's budget includes an additional $6.51 million for this program. This amount is insufficient to meet even the requirements of the researchers at government hospitals and laboratories and is insufficient for the nationwide program of drug development and clinical trials. Absence of such trials is responsible for attempts of U.S. citizens to attempt to obtain therapy abroad.

A Program of Epidemiology - no increase

The current program of epidemiological survey and of transmission studies is excellent and necessary. A continuation of these programs at or near the present level is needed. These efforts are now targeted for $32,000,000 per year.

The Secretary's budget request of $14 million for additional epidemiolgy and public education to be co-ordinated by the Centers for Disease Control is adequeate for the task.

A Program of Public Education

Public education regarding the nature of the disease and modes of transmission will be urgently needed as virus infection and disease spreads throughout the population. The effects of the epidemic on the social organization, health care costs, insurance costs, and the medical delivery system will be major.

The Current Costs

Medical costs are now about $100,000 per AIDS victim. Medical costs for patients who suffer brain disease, cancer or combinations of any of the symptoms are likely to be higher.

For AIDS alone the costs of the 10,000 AIDS cases so far diagnosed will be one billion dollars. The next year there will be 15,000 - 20,000 new AIDS victims. Loss in terms of lost productivity is much higher.

ORGANIZATIONAL NEEDS

A national co-ordinating task force with authority to direct research and development programs should be established. The group should be comprised of leaders in the field of research, medicine, and epidemiology. The task force should be drawn from leading governmental and non-governmental experts. The task force should have oversight responsibility over governmental and non-governmental programs.

Five co-ordinating committees that report to the task force should be established in areas of fundamental research, vaccine development, therapy, epidemiology and public education. The co-ordinating committees should have the responsibility for the rapid review and funding of projects. These groups should encourage initialization of projects. The groups should co-ordinate both intra-agency as well as non-governmental activities.

SUMMARY

New organization and increased funding is urgently needed to combat the HTLV-III virus. Specific recommendations include:

-Creation of a national task force comprised of citizens and experts from within and outside the government to guide policy

-Creation of programs to coordinate inter-governmental and non-governmental development and funding in the areas of fundamental research, vaccine development, therapy, epidemiology, and public education

-Increase in the current funding level to $236.25 million for the next fiscal year.

Specific Proposals include:

Secretary of Health Fy´86 Budget		Proposed New Budget	
Center for disease control	45.6	45.6	+0
NIH	70.56	179.56	+110
FDA	6.63	6.63	+0
ADAMHA	3.46	3.46	+0
	126.25	236.25	+110

A National Task Force to oversee and to implement inter agency and non-government efforts should be established. Five program co-ordinating groups with the authority to initiate, review and find new efforts in areas of fundamental research, vaccine development, therapy, epidemiology and public education should be established.

STATEMENT OF DR. MALCOLM A.S. MOORE

As an active member of the biomedical research community I wish to address a number of issues in what has come to be called the AIDS crisis from the perspective of a research investigator who has participated in some of the research areas relevant to the understanding of the basic biology of AIDS and in approaches that may prove of value in the development of clinical trials of new therapeutic strategies. I speak from a personal perspective as to how I perceive the impact of the problem of AIDS on the resources, financing, manpower etc. of biomedical science in this country, not as an expert on AIDS itself, but as a biomedical scientist in the areas of immunology, hematology and cancer. It is critical to determine if the nature and extent of federal support for biomedical science has enabled us to cope rapidly enough with the AIDS problem and whether the infusion of additional money or the redistribution of existing funds would have a significant impact on the development of a cure for AIDS. The allocation of Federal sources to fundamental biomedical science by world standing can be construed as having been generous although warning signs are being raised about its gradual erosion by inflation and other causes of our national research and clinical base which must be maintained in order to be flexible enough to cope with the present health crisis of AIDS and undoubted future health crisis.

Placed in perspective, as Dr. Ludwik Gross did in his overview of a major symposium on HTLV held at the NIH less than a year ago, it is anticipated that in a total population of 230 million in the USA, we can anticipate 870,000 cases of malignant tumors this year alone, including 65,000 new cases of leukemia and other malignant diseases of the blood forming tissue (Cancer Research Supplement 45 No.9, Sept. 1985). By the beginning of this year nearly 7,000 cases of AIDS had been reported to the CDC., and rates among single (never-married) men 15 years or older approximated 200 per 100,000 population in high risk areas such as Manhattan and San Francisco with a two year mortality rate exceeding 80%. Through its geographical location and the high incidence of malignancies (Kaposi's Sarcoma and lymphomas) associated with AIDS, a large number of AIDS patients have been seen and treated at Memorial Sloan-Kettering Cancer Center since the disease was first reported. Obviously such a burden is difficult to sustain by any single institution and the clinical care and management of patients with AIDS, and in particular the initiation of large scale controlled Phase II trials of anti-viral and immunostimulatory therapy with various lymphokines should be undertaken as collaborative efforts initially among tertiary care centers in specific geographical regions with high AIDS incidence and later with supervised protocols in a general hospital environment.

In dealing with the past and future support mechanism for AIDS research both basic and clinical, the following points can be made. The outstanding progress in identification, isolation and characterization of the causative agent of AIDS-HTLV-3- and its mode of transmission was supported by federal funding for very basic molecular biology, virology and epidemiology, but it should not be forgotten that major breakthroughs evolved from the funding of the Cancer Research Program in the course of a search for human cancer or leukemia producing viruses.

The scientific nature is an inquisitive one and as observations, frequently serendipitous, are made even in a highly focussed program such as the search for human tumor virus, the flexibility of our current system has allowed the identification of the non oncogenic virus of AIDS and discovery of growth factor for normal T lymphocytes. This T cell growth factor, Interleukin- 2, proved critical for normal T cell growth and greatly assisted in the isolation of the AIDS virus and has probable value in AIDS therapy.

The research activities of my colleagues and myself began with attempts to understand the origin of the T lymphocyte population, the role of the thymus gland and of the precursors (stem cells) of all blood forming cells including lymphocytes. This basic research, supported by CA, AI and HL agencies via conventional RO1, RFA and program project grant support mechanisms, led us in 1981 to succeed in the first purification of human Interleukin-2, first discovered in 1976 in the laboratory of Dr. Gallo at the NCI as a biologically important growth factor for T cells Our preclinical studies that were confirmed and extended in many other laboratories demonstrated that the lymphocytes of patients with AIDS were defective in production of this Interleukin-2 growth factor. Furthermore, it was possible to demonstrate an impairment of the mitogenic response of lymphocytes from patients with AIDS particularly to the monoclonal antibody OKT3. It should be noted that the development of the technique of producing monoclonal antibodies of exquisite specificity evolved from basic research in immunology and provided a powerful tool permitting the detection of derangements of specific subsets of lymphocytes in patients with AIDS. Monoclonal antibodies also assist in monitoring T cell populations in clinical trials. Other defects that we and others have noted in AIDS involved natural killer cells, lymphokine activated killer cells and antiviral cytotoxic T lymphocytes. All these defects were correctable to varying degrees by brief exposure of the patient's cells outside the body to Interleukin-2. Interleukin-2 clinical trials have not yet proved efficacious in AIDS, possibly because the very cells proliferating in response to Interleukin-2 are also the cells susceptible to infection and destruction by the AIDS virus.

Other innovative approaches that have shown promise in vitro have involved various procedures that interfere with the replication of the AIDS virus, for example Suramin, an anti-protozoan drug, and various nucleoside analogues. The toxicity of these agents, and their failure to lead to direct recovery of T cell function, suggests that future clinical trials should involve combinations of agents with anti-viral properties and immunostimulatory features. This combination biotherapy may conceivably be extended by the inclusion of other naturally occurring products of T cell activation that influence the function of a number of different host defence cells against bacteria, parasites, and viruses. Recombinant DNA technology has made available a variety of such lymphokines including interferons and neutrophil and macrophage growth and activating factors. Research in my own laboratory and in other centers leads us to believe that complex interactions between these natural growth factors are critical to a normal immune status and to achieve this goal in AIDS would be the objective of a series of clinical trials based upon information gleaned from in vitro studies of AIDS patients.

The mechanisms developed by the National Cancer Institute over the years for clinical trials of conventional chemotherapeutic agents, and more recently the guidelines proposed by the biological response modifier Decision Network Committee, provide a clear blueprint for a comparable clinical trial organisation in AIDS with a Phase IA study to determine toxicity and a Phase

IB to closely monitor parameters readily measurable as indicators of response (e.g. changes in viral titer, restoration of T4 cell function). Rapid progression to Phase II trials in relatively small groups of patients in a limited number of specialised centers should then be followed by extensive cooperative or regional collaborative trials.

We are not going to cure AIDS by the simple expedient of indiscriminately throwing more money at it. The temptation to increase the number of scientists and clinicians participating in AIDS research by any simplistic expedient such as being excessively lenient in the fundable priority scores established by peer review study sections in grants focused on AIDS would attack the validity and importance of peer review and the succes it has already had in supporting the inovative research currently underway in AIDS . Furthermore, the introduction of funded proposals of dubious merit undertaken by investigators with limited qualifications in unfavourable environments would not, as suggested by some, increase the possibility of a chance, unexpected discovery. For some years I have been a Trustee of the Leukemia Society of America and a Member of its Board of Medical and Scientific Advisors whose role is to review scientific quality of applications. This is a disease focused private organization but we have held to a firm philosophy that very fundamental research (for example in the genetics of fruit flies) if of high scientific quality could have potential for improved understanding of the leukemic process. Furthermore, the cut off point for support by this Society is based strictly on scientific criteria, rather than funds available. This organization, like the Federal Agencies, has elected always to go with quality over quantity.

Serendipity has always played a crucial role in new medical and scientific advances (e.g. the discovery of penicillin) but only in the context of highly qualified scientists and/or research environments capable of recognizing and capitalizing upon such chance observations. Such an infrastructure exists within the current federally supported system and should not be weakened or diluted. The analogy of an infinite number of monkeys with an infinite number of typewriters in an infinite time writing Hamlet or producing a cure for AIDS is counteracted by the problem of accumulation of disinformation, premature expectations and outright error based on faulty experimentation and inadequate clinical design by underqualified investigators. This would clearly be counterproductive to our effort.

As a former member of an NIH study section reviewing a broad range of immunological grant proposals and as an informed outsider in the AIDS area, enough promising leads appear to exist already and funding should be focussed on the rapid expansion of these current endeavours, particularly clinical trials, so that we can focus rapidly upon the most therapeutically attractive options.

Mandatory information exchange between federally-supported investigators should be strengthened and some form of oversight committee (or individual) should be formalized so that the federally sponsored effort speaks with one voice to the public and the patients and will act as a central repository of all information on the disease. Misinformation, disinformation and misunderstandings abound, as do false expectations. The public should understand that dramatic developments have taken place in understanding AIDS, one of the greatest feats in medical science of this century, but the public must be better informed on such controversial issues as the communicability of the disease and the time constraints and complexities of bringing new drugs or therapies to general clinical use.

In looking at the quality and numbers of biomeidical investigators trained in the immunological, biological, virological and molecular aspects of AIDS and in the clinical care of AIDS patients, it is fortunate that federally supported post-doctoral and clinical training programs have in general provided the qualified individuals needed to tackle the AIDS crisis. The importance of continuity in such training programs must not be overlooked.

STATEMENT OF DR. DON C. DES JARLAIS

I would first like to thank the Committee for this opportunity to testify regarding research on AIDS among intravenous (IV) drug users.

Intravenous (IV) drug users form the second largest group of persons who have developed AIDS in the U.S. Of the 13,216 adult cases of AIDS reported to the Centers for Disease Control through Sept. 20, 1985, 3393 have occurred in IV drug users, including 1144 IV drug users who also have a history of male homosexual activity. The present hierarchical risk classification method used by the CDC does not distinguish male homosexual IV drug users from other male homosexuals, and thus tends to underestimate the numbers of IV drug users with AIDS.

IV drug users are important not only because of the number of them who have developed AIDS, but also because they form the primary linkage to two other groups at increased risk for the disease. Of the 186 children who have developed AIDS, 98 (53%) have had an IV drug user as a parent. Of the 133 persons who appear to have developed AIDS through heterosexual transmission, 97 (73%) have involved transmission from an IV drug user. (Data from the Centers for Disease Control, through Sept. 20, 1985.) Thus control of the epidemic within the IV drug user group will also lead to great reductions in the number of children and heterosexual partners who are likely to develop the disease.

It is fitting that these hearings are being held by an appropriations committee. In addition to the incalcuable human suffering of those who have developed AIDS, and the fears of others for both themselves and their loved ones, AIDS is exacting a large financial toll on our society. Estimates of the cost of treating a single case of AIDS in New York City range from $40,000 to $160,000, and the number of cases continues to increase exponentially. Current expenditures on research and prevention may well produce very large savings in the next few years.

I will first review our current research on AIDS among IV drug users, and then outline what I see as needed areas for additional research. Before discussing the content of our research, I would like to acknowledge my colleagues at the Narcotic and Drug Research, Inc., New York Univerisity Medical Center, Beth Israel Medical Center, Manhattan Veterans Administration Medical Center and the Centers for Disease Control. I would also gratefully like to acknowledge support from the National Institute on Drug Abuse, which has been the primary sponsor for our research. Additional support has been provided by New York State, the Centers for Disease Control and the New York City Department of Health. Our research has included studies of the epidemiology of HTLV-III/LAV (the virus that is the primary cause of AIDS), the natural history of HTLV-III/LAV infection in IV drug users, and efforts undertaken by IV drug users to reduce the risk of developing AIDS.

Epidemiology of HTLV-III/LAV

The development of antibody tests for exposure to HTLV-III/LAV has greatly improved our ability to conduct epidemiologic studies of AIDS among IV drug users for several reasons. Previously epidemiologic research had to use actual cases of surveillance definition AIDS as a dependent variable. The long and variable time period between viral exposure and development of the disease and the high ratio of exposed persons to AIDS cases at any single point in time both make numbers of exposed persons a much more powerful variable for analyis than numbers of AIDS cases. While the antibody tests are excellent for research purposes, where group data is used, and for screeening blood donations, there are limits to their usefulness with IV drug users at the individual level. Repeated tests of the same serum samples from IV drug users often show conflicting results, making problematic any action to be taken with a specific individual.

It is clear that the sharing of needles for injecting drugs is the primary method of transmitting HTLV-III/LAV virus among IV drug users. In terms of viral transmission, "needle sharing" should be defined to include the sharing of the syringes used for injection, and possibly even the "cookers" used for preparation of the drugs. Heroin and cocaine are by far the most commonly injected drugs among IV drug users who have been exposed to the HTLV-III/LAV virus, but the particular drug being injected does not appear to play an important part in the spread of the virus. Persons sharing needles to inject amphetamines or other drugs must also be considered at risk for viral exposure.

In the United States, the AIDS epidemic in IV drug users is centered in the New York City metropolitan area. Our 1984 studies of HTLV-III/LAV seropositivity among IV drug users in New York City showed an average of 59% of the IV drug users had been exposed to the virus. This did not vary significantly among subjects recruited from methadone maintenance, detoxification or therapeutic community treatment programs. Our collaborative studies with Onishi and colleagues in San Francisco, and Bokos and colleagues in Chicago found approximately 10% positive in these cities. Clearly the AIDS epidemic among IV drug users is most advanced in the New York City area, but it has also begun in other cities with large numbers of IV drug users. Prevention efforts are needed throughout the country, but particularly in areas like San Francisco and Chicago, where the great majority of IV drug users have not yet been exposed to the virus.

We have also conducted historical studies of the epidemic in New York City, using serum samples that were originally collected for other purposes. We have samples of serum from IV drug users that go back to the middle 1960's. The first indication of HTLV-III/LAV antibody presence was found in a sample from 1978. Seroprevalence increased steadily in later samples--30% of the 1979 samples were positive, 40% of the 1980 samples, and 50% of 1982 samples. The HTLV-III/LAV virus appears to have been introduced to IV drug users in the late 1970's in New York City and the seroprevalence rate has increased by about 5% per year since then.

Natural History of HTLV-III/LAV Infection

The course of HTLV-III/LAV infection after a diagnosis of AIDS has been well studied, but there is comparatively little knowledge of the early "natural history" of HTLV-III/LAV infection among IV drug users who do not (or have not yet) developed surveillance definition AIDS. Important aspects of the natural history yet to be determined include significant events in the early course of the infection, the different possible outcomes for IV drug users exposed to the HTLV-III/LAV virus and the distribution of exposed persons across the different outcomes.

We are currently following a group of 358 IV drug users, the majority of whom have been exposed to HTLV-III/LAV. This will permit us to monitor the early course of HTLV-III/LAV infection as well as to determine the various possible outcomes. The decline of T4 (helper) cells to an abnormally low level appears to be an important marker in the infection process. This event is associated with a variety of changes in immunologic status, including increases in serum immunoglobulins and serum beta-2 microglobulin, and increases in AIDS-related symptoms. It may mark the point where serious impairment of the immune system begins, and after which treatment may need to include reconstitution of the immune system as well as halting HTLV-III/LAV viral replication.

Surveillance definition AIDS and AIDS-related complex (ARC) are the two best known outcomes of HTLV-III/LAV infection, but certainly not the only possible ones. Most IV drug users exposed to HTLV-III/LAV will probably not develop AIDS or any other significant health problems as a result. There is, however, increasing evidence of direct HTLV-III/LAV effects upon the central nervous system, leading to a syndrome that resembles Alzheimer's disease. There have also been epidemics of non-AIDS pneumonia and tuberculosis among IV drug users in New York City that coincide with the AIDS epidemic, and some indications of increased rates of endocarditis among IV drug users exposed to HTLV-III/LAV. It is important to determine if exposure to HTLV-III/LAV does increase susceptibility to these other serious illnesses that are not normally associated with AIDS. Given the large number of persons who have already been exposed to HTLV-III/LAV, it is important to have knowledge of the full range of possible outcomes from exposure.

One of the most frequently asked questions regarding the natural history of HTLV-III/LAV infection is the likelihood of developing AIDS. The most common estimates center on ten per cent of those exposed developing surveillance definition AIDS. In our present study we have found 2% developing AIDS within the first year of follow-up, which is consistent with an overall estimate of ten per cent. In light of the other possible outcomes noted above, many of which are disabling or fatal in themselves, the percentage of persons who develop severe health problems as a result of HTLV-III/LAV exposure will very likely be much greater than ten per cent.

Co-Factors

Our follow-up of HTLV-III/LAV exposed IV drug users is also being used to examine possible co-factors that might influence the progression of HTLV-III/LAV infection. Given the absence of effective treatment and the existence large numbers of persons who have already been exposed to the virus, identification of co-factors may have great potential for reducing the adverse consequences of viral exposure. If co-factors involve modifiable behavior, then it may be possible for many persons who have already been exposed to take actions that would reduce the chances of adverse outcomes.

The potential co-factors that we are examining include continued drug injection/repeated exposure to the virus, exposure through multiple routes, use of non-injected drugs (particularly alcohol and marijuana), stress, and other illnesses. Our preliminary findings indicate that multiple exposure to the virus may have deleterious effects, and recommendations to persons who have already been exposed should advise against activities that may lead to additional exposures.

Risk Reduction

There is a common stereotype that IV drug users are not at all concerned about health, and are not likely to change their behavior in order to avoid exposure to HTLV-III/LAV. Much of the stereotype appears to be based on observations of "shooting galleries," where needles can be rented for injecting, and are often quite unsanitary. Despite this stereotype, there is consistent evidence from a variety of sources to show that IV drug users in New York City have changed their behavior in order to reduce the chances of exposure to the AIDS virus.

We have conducted studies of IV drug users in treatment, IV drug users not in treatment, and of persons selling needles for drug injection. All of these studies showed that IV drug users in New York City knew of AIDS, and the great majority (approximately 90%) knew that it was spread through sharing needles. Approximately 60% of the subjects reported having made efforts to reduce their chances of exposure to the AIDS virus, primarily through increased use of sterile needles. This self-reported increase in sterile needles was confirmed in our interviews of persons selling needles, who reported an increase in demand for sterile needles as a direct result of the AIDS epidemic. Limited availability of sterile needles was also noted as a major constraint on risk reduction in our studies of IV drug users not in treatment.

It is not yet possible to quantify precisely the amount of reduced needle sharing that has occurred among IV drug users in New York City. Drawing a truly random sample of IV drug users, and then monitoring their behavior over time, would be an enormously complex research undertaking. All of our present evidence, however, does indicate that efforts to reduce transmission of HTLV-III/LAV are occurring as a result of knowledge of AIDS. IV drug users should not be considered unresponsive to the threat of AIDS.

Needed Future Research

Treatment, Natural History and Co-factor Research. There has been a recent concern in the media about the relative lack of funding for treatment for AIDS. While there are clear needs for additional studies, there are also problems that can be created by artificial distinctions between "natural history" and "co-factor" research compared to "treatment" research. Given the nature of HTLV-III/LAV virus, treatment research is most likely to produce results if it is based upon findings from natural history and co-factor studies. One of the most discouraging aspects of treatment for AIDS is that it appears that by the time a person is diagnosed with surveillance definition AIDS, the immune system may have already suffered major impairment. Thus treatment not only has to contend with the immediate opportunistic infection or Kaposi's sarcoma, and halting replication of the virus, but also reconstituting the immune system. Treatment that begins prior to diagnosed AIDS may have a much higher probability of success. The presently envisioned treatments are based primarily upon anti-viral drugs, many of which have serious side effects. Thus selection of persons to receive a given treatment involves a careful trade-off between possible benefits versus potential harm from the treatment. Studies of the natural history of HTLV-III/LAV infection may help identify particular stages in the infection process where treatment is most likely to be beneficial to the patient.

Similarly, studies of potential co-factors may identify actions that persons exposed to HTLV-III/LAV may take to lessen the chances of adverse outcomes and reduce the need for treatment. Rather than seeing treatment research as separate and competing with other types of AIDS research, it is important to recognize the interdependencies among the different types of AIDS research.

Prevention. It should be emphasized that AIDS is a fully preventable disease. The major modes of transmission of the virus are sufficiently well known, and even within these modes transmission is relatively difficult. Current research has shown behavior change to reduce risk of transmission does occur for both male homosexuals and IV drug users, the two largest increased risk groups. This research has also shown that the risk reduction resulting from knowledge of AIDS is not complete. IV drug use and sexual behavior are difficult areas of behavior to change. The next stage of prevention research will need to go beyond mere providing of information and examine additional methods for risk reduction.

For the IV drug use risk group, the needed areas for prevention research include study of new forms of large scale treatment, factors affecting the availability of sterile needles and recruitment into drug injecting. This last area may hold particular promise. To the extent that we can develop new ways of keeping youth from starting to inject drugs, we will not only reduce transmission of HTLV-III/LAV, but also prevent a variety of other health and social problems. Again, I would like to note that our preliminary studies in this area indicate that mere knowledge of AIDS is not likely to be sufficient.

Societal Reactions to AIDS. The area related to AIDS that has received the least amount of research support has been societal reactions to the AIDS epidemic. While opinions are frequently voiced regarding the reactions of different parts of society to the epidemic, there is a paucity of scientifically collected data on the subject. It would be wrong to assume that societal reactions can simply be ignored or that they can be appropriately handled through disseminating rational information and relying on common sense. The recent school strike and lawsuit in New York City illustrate only one of the types of problematic societal reactions to the AIDS epidemic. One of the more disturbing aspects of this episode was a New York News poll showing that 55% of the respondents did not want children with AIDS attending school even if the health authorities could completely assure the safety of other children. It is clear that there is a potential loss of credibility of public health authorities over the AIDS issue.

Furthermore, preventing the spread of AIDS involves behavior changes that are often difficult to make. Some public reactions may be counterproductive in that they increase the difficulty of making these behavior changes. Employment discrimination based on membership in the present risk groups is an example. For drug users, obtaining employment is often a central aspect of successful treatment. Discrimination in employment against ex-addicts could undermine treatment efforts, leading to increased drug use, and, most probably, to increases in the number of cases of AIDS.

Public reactions thus far have focussed on persons who have AIDS. If this focus should change to persons exposed to HTLV-III/LAV, then the potential for hysteria and other non-adaptive responses will increase by at least an order of magnitude. We will need a research capability that can provide a thorough understanding of public reactions and suggestions for minimizing dysfunctional consequences.

Summary

Again, I would like to thank the subcommittee for this opportunity to present our current reasearch on AIDS among IV drug users and suggestions for directions of future research. IV drug users have not received the same amount of public attention as other groups at increased risk for AIDS. They do, however, form a large group, and one where research and prevention efforts may be particularly important.

Dr. HASELTINE. I think the previous speakers have highlighted what amounts to our current and very serious battle of man versus micro. It is a battle that we as a species have fought many times before. We won the battle before. I fully expect we will win this particular ground. However, if you are scoring points, there are many more points on the other side than there are on ours.

What I am here to do today is give you a very brief overview of the perception of the scientist not working within the Government, rather outside the Government apparatus at Harvard University, about the progress that is being made, what we might do in the future to speed progress along, and I will particularly, to let you know where you are going, make a case in certain areas the funding is not adequate to address some of the needs, particularly in the areas of fundamental research and mobilization of our biomedical community.

I will say it is certainly no fault of any of the people who are here. Quite the contrary. They are dedicated. They have done their best in this effort. What we all see with the AIDS problem is a rapidly emerging picture and an unfolding one for we at the forefront of science as well as for the public.

I don't blame everyone being confused. What everyone must have is multiple exposure to the information the scientific and medical community has what we knew 2 years ago, what we knew 6 months ago, what we know today. It is an unfolding picture. For that reason, there is some reason for confusion among the public.

Let me say I am in total agreement with the seriousness of the problem as it has been expressed by the previous panel members.

Let me put it in a little different light. There are probably, conservatively speaking, 1 million of our fellow citizens infected. Worldwide, there may be 2 million people infected already with this virus that occurred from no infections 20 years ago.

One out of ten Africans in the central part of the continent are infected, that is, the adult population, amounting to some 10 million people. The disease in this country is spreading at the rate of 1,000 to 2,000 people a day. The disease is a disease confined not only to our public sector but also to the military and all elements of our society.

Although the disease first made its appearance in the homosexual community, everyone, I think, is in agreement this is not a homosexual problem; it is a problem for all human beings. The virus does not respect people by race, sex, or sexual preference. We know once infected, the prognosis of everyone, children, women, and men, is equally bleak.

Similarly, we know there are probably no particular sexual practices. Those that were initially associated with this disease are those prevalent in the population that was first noticed, that is the homosexual practices.

The virus has been documented to be transmitted heterosexually from women to men, from men to women and certainly as you have heard from woman to child.

With respect to one other feature, I would like to address and that is how much is this a disease of men versus women? In this country today, the numbers that were apparent but not stated absolutely, there are probably at least 75,000 women infected in this country today. One out of ten people who suffer from the obvious and most serious disease symptoms of AIDS in New York City are women. This is not a problem restricted to the homosexual population. It is a problem that will affect all of us.

Senator D'AMATO. Could I ask you a question? What is this women/men ratio in New York?

Dr. HASELTINE. The ratio I think reported is 14 to 1 in this country for men to women. In Africa, it is 1 to 1. I think that is probably not a reflection of the preference of the virus. We know in Africa and other places it affects men and women equally. The rate at which a virus like this spreads through our population depends on the fraction of the population that is extremely active sexually. That fraction is higher in the homosexual population. However, that fraction also is in the heterosexual population and it is that factor, how many people are very promiscuous which will set the rate at which this virus will and is spreading through the heterosexual community.

Where will this disease go in our society? We know the virus can be spread through prostitution. A recent study in the Army confirmed that, as other studies from the Centers for Disease Control. We know the first presentation of this virus is inapparent. That represents the most serious threat of this infectious agent. There is a carrier state.

In fact, for every person who has obvious symptoms, there are at least 100 people who don't have symptoms who are carriers who can transmit the disease possibly better than the others.

In diseases like this, we look to an allergy, we look to other inapparent venereal diseases. I bring to mind chlamydia. We find that one-third of our college girls are infected with that disease. This is the kind of potential we are looking at if this is to be viewed as a war between men and micro.

What can we do? We can count the bodies. That is pretty well but not entirely done. I referred to the blood tests. You are measuring how many people are infected. If someone is interested, I would tell you the strengths and weaknesses of that blood test.

Second, you can treat the wounded. That is going, as I will outline briefly, to be an extremely difficult task.

Finally, you can prevent the war. That would be vaccines or chemical prophylactic treatments. Both of those in and of themselves are major undertakings. Given time and resources, we can achieve those goals, but we are very far today as you have heard from those.

Everyone of the panel members has said, and I wish to underscore, we have no treatment for this disease, nor is there any in the immediate prospect. We have no vaccine for this disease, nor is there any in the immediate prospect.

Why is it that we give you such a bleak prognosis about vaccines or about treatment? We have heard also that despite the fact there is this bleak outlook, there has been remarkable progress and I should underscore that. Never, I think, in the words of many people have we ever seen such a rapid mobilization of our scientific community to such a disease, not only recognize what the infectious agent is, we have cloned it, expressed it, tests have been developed to determine who is infected, who isn't and we are now beginning, I just stress beginning, to assess the impact on the body. The fact that such rapid progress has been made is attributed to the foresight of this committee, the Congress, and the health apparatus in the country.

As our chairman said, without this, we would be starting it at the first yard line and not at the 40-yard line. We still, as you know, have a long distance to go from the 40-yard line to a touchdown. It is about that distance that I now wish to speak.

Why is it when we say there has been so much progress that we then say in the same breath that we don't know when or if a vaccine will be present. We don't know when or if a treatment will be present. When we take a little bit closer look at the progress that has been made, and I should tell you I have been involved from the beginning in studies of this virus and its structure and function, we see the progress we make is the easiest kind for scientists to make, it is progress by analogy.

We knew about viruses and we isolated a virus. We knew about genes these viruses have and are able to study those genes.

Where we have made the progress is those areas we already know a great deal about. However, that for scientists is the beginning of the problem. What we now have to do is forge ahead into those very difficult areas of the unknown, and that is where we are now. We have made the progress that is easy. By way of example, let me give you a few notions of what I mean by making the progress that is easy.

We know how to isolate and clone viruses. We have, by virtue of our techniques, developed for a long time. However, when we look at the structure of this virus, actually what was done was a very clever fishing expedition by people at the National Cancer Institute and other places that looked for a virus similar to what causes leukemia.

What came out of that net was a very different beast, indeed. It was not the virus we looked for. It is a surprise and it is going to take us a long time to figure out why that particular fish came out of that particular net.

Be that as it may, we now know where most viruses have three genes, this has six. I and other colleagues found the sixth. We have not yet mapped the terrain.

Let me liken this to what Columbus did when he sailed West. He thought he was going to India. What he found was this continent. We have a new world to explore and that is to rid the world of this virus. There are more pieces to it than we thought, and we don't know what to do with them. It has taken us 20 years to figure out what those first three genes have done, 20 years of research through our best scientists throughout this country and throughout the world.

We are confident we have better techniques to figure out what these other three genes are doing, but we don't know when for sure that will be.

We are also in another gray area of the unknown. Just how about the virus goes about doing what it does we don't really know. How a virus affects the body, what the immune system in response to that virus is we don't really know.

As little as 3 or 4 months ago, people would tell you it affects oneself in the immune system. As we know, it affects many cells, referring to what is called knocking off the conductor of the immune symphony, you would now find somebody is murdering people in the string and horn section as well.

We are finding cells we didn't think to be infecting to be infected.

I think the most serious and long-range implication of our new knowledge is we must regard this as infection of the brain maybe even more so than infection of the immune system. We now know from studies at Harvard, when this virus enters the body, it probably goes to the brain as soon as it affects the person. There it works a steady, possibly irrevocable series of damages. We believe perhaps the immune effects are not what the virus initially intended. It appears the virus jumps into monkeys where it doesn't cause them much harm. It probably affects some parts of the immune system and arrives from the immune system into the brain.

We now have a model to look at. In those models, infection with the virus is life long and disease is progressing. This bears on your question, Senator D'Amato, as to what the prospects of people affected are. They are probably extremely bleak.

The numbers you heard represent not only the numbers cited here, but other studies from around the country that after 5 to 7 years, 30 percent of the people infected have AIDS, far greater up to 50 percent have other life-threatening illnesses. We don't know in the end if the serious symptoms of the disease will come in sight. With every year that passes, the ability of this virus to wreak havoc in our body becomes more apparent in time.

If it is like the other viruses, it is a oneway path of destruction throughout the lifetime of the animal.

We may be looking in our search for vaccines and for theories. After all, some of the greatest advances made in medical science were based on luck. Pasteur found the vaccinia virus and vaccines were developed. People were able to develop vaccine for yellow fever in an experiment which has never ever been possible to duplicate. Maybe we would be lucky, but I wouldn't want to count on luck in this kind of disease.

What must we count on? Well, we have as a species three things we can do. We can communicate; we can organize; and we can think extremely well.

Communication, I don't think, will solve the problem. It is crucially and vitally important, as you have heard, but we know what the limitations to communication can be, even for things like cigarette smoking.

You don't stop people's habits. Here we are talking about sexuality and drug abuse. How big an effect do you think communication will really have on putting a dent in sexuality and in drug abuse?

Some but not entirely to cure the problem. Therefore, for example, look to our forebearers, they knew how to get syphilis. The best among them got syphilis and died of it. I think that is what we are looking at. We can communicate, reduce the rate at which it will spread, but we will not stop the spread.

We must then provide scientific problems. As I looked at this I outlined the many fundamental areas of research and lack of knowledge we have. Compare that to the effort we have mounted for our biomedical community. We have, as I said before, due, in great measure to your efforts, the most splendid biomedical research community ever assembled, certainly the best one in the world today.

How much of that effort has been marshaled to this disease? If you really look at it, the answer is a very small fraction. Why is that? The people you heard talk today, they have, in fact, been immobilized extremely effectively. I would say they have done everything they can do within their budgets, and even more. For example, the current vaccine programs underway are being done today, almost pro bono. If you ask me, do they need more money for vaccines? Yes; ask them, they will tell you yes or maybe yes.

Therapy, I would say the same. If I look at what they are doing to therapy, I see heroic efforts done on a shoestring. I don't think that is the way even a Government program should be run. They should be run with lots of funding, lots of coordination. We need a lot more funding, in my opinion, both for vaccine development and for clinical trials nationwide, and if you look at those moneys and they can give you a good idea of how much it takes to push through a single drug, that estimate is at least $50 million and probably a lot more over time.

Although you have heard there are encouraging efforts, in my opinion, these are shoestring efforts that should be systemmatically reviewed and should be encouraged. I encourage you to consider additional funding.

Another area I can speak with much more confidence because I looked at that and looked at my colleagues outside the Government. Most of our biomedical science community is outside the Government. We have splendid research institutes throughout the length and breadth of this country. To what extent are those mobilized to this problem?

Let me take you on a tour of the country and spotlight the premiere institutions and what research is being done.

Harvard, there are four first-rate labs working on it. That is about it. MIT, nothing; Tufts really not much; Boston University virtually nothing. In Senator Weicker's State, Yale, the best pharmacology group in the world, probably not a single person there working on AIDS. There is some clinical work but not fundamental, first-rate science of the kind needed to make breakthroughs. University of Connecticut the same thing. Not that people are not working.

Let's move down to New Jersey. Let's look at Princeton. We see almost nobody is working in Princeton on these problems. New York City. Sloan-Kettering is doing good work but the best scientists at Columbia, New York University, Mount Sinai are not fully engaged in these problems.

We look down further, the University of Virginia, same situation. Fortunately, at Duke we have a very fine medical center, people working, a couple of good people are working in Miami.

Midwest of this country, it is a virtual desert insofar as first-rate fundamental research on this problem goes. If you look at the west coast, you see several centers. You see San Francisco, UCLA. You don't see Seattle; you don't see Oregon; you don't see Berkeley; you don't see Stanford working on this problem in a real way. Why is that? How do you get our best scientific minds engaged in such an effort and you have to realize, as you well know, what the situation has been for our first-rate scientists. They are coming out of a traumatic period which you were very much a part of.

That is one-fourth of our grants were attempted to be taken away by OMB manipulations. You successfully restored part of that. There is shock, there is trauma that comes as part of the overall contrast in the overall biomedical community. That has had a serious effect on keeping the best scientists who already demonstrated they can work on. They have a clean track. If they try and go into new and different scientific turf, they often have their hands slapped. Many grants on AIDS are reviewed today as on a business-as-usual basis.

I would urge you to consider a review process which speeds funds which are available in this area, speeds the review. I am sure everyone of you heard every scientist sitting here say we need more research.

Your question is why is this different? It is different because the problem is different. What goes through the mind is the question is money in fundamental research really necessary and can it be spent? I would argue we are now at the stage with the research that now is the best time to attract more of our best minds into this area. Why is that? We have a very good view of the problem.

Two years ago, we didn't have the virus. This year we would. Two years ago, we didn't understand the immune effects in any real way. Now we do. Two years ago we didn't know what goes into the brain. Now we do. We have a view of what is needed. What we need are more resources in this area, more resources not only for the Government scientists, but scientists working outside the Government.

Let me say that, finally, one area I would like to discuss in addition to the civilian population are the problems which are inevitably occurring within our military populations as well.

As the problems of AIDS spread through our population at the rate of 1,000 or 2,000 cases a day, we will face military manpower problems. Today, if you vaccinate a soldier with AIDS or incipient form of it, it is likely you will kill him because of the massive dose of immune innoculation.

We will have a manpower problem in the sense if we need to maintain our troops abroad in areas where the virus is epidemic.

Let me point to the city of Berlin where 50 percent of the prostitutes are affected. In June 1985, a recent report from the military found that 5.4 percent of our soldiers who go to venereal disease clinics are infected. Those are not homosexuals but normal young guys who visit prostitutes. One-half the prostitutes are infected and those guys are infected. They will bring the viruses home to their wives, to their families. We are dealing with what must be considered a venereal disease. The Army looks at it that way. The CDC is now looking at it that way.

Let me point out what is going to be a major, serious threat to the heterosexual population is the prostitute population. What is your chance if you go to Manhattan of encountering an infected prostitute? It is one in five today. Boston, one in five.

Many of the customers of prostitutes are upstanding citizens who go home and bring that virus into their families; their wives will transmit that to their unborn children.

We are facing a major problem. I don't think we are organized in an effective way to use our strengths, the strengths that we have in our biomedical community to combat this.

Thank you.

Senator WEICKER. Thank you very much, Dr. Haseltine. I appreciate your testimony. I think we will ask each one of these witnesses questions as we move along since each represents different points of view.

First of all, let me say this. I greatly appreciate your taking the time to give your thoughts on this matter before the committee. Your credentials are impeccable. Obviously, weight has to be given to both fact and opinion which you set forth before us. I am not prepared to go ahead. Indeed, I am only here to listen to the matters of science which I discuss. I am not a man of science. I am here to listen.

On the other hand, I think I can comment on the appropriation processes and what has gone on so far as money is concerned.

First of all, I think you realize as well as anybody else, I do not sit in the bosom of this administration. [Laughter.]

I have been known to have more than one disagreement with them.

Senator D'AMATO. Really.

Senator WEICKER. Of matters that come before the committee, especially insofar as the funding of the scientific research is concerned. But having said that, on the matter of funding for AIDS, we have worked closely together, as indeed has the House Committee. I think it is especially important to cite here, even many people don't know, the excellent relationship which I enjoy not only with Dr. Wyngaarden but the various heads of the institutes over at NIH.

These gentlemen have both publicly, because I remember very well Dr. DeVita's remarks in the first hearing I chaired 2 years ago, not hesitating to have our relationship based on total candor. They don't take their orders from the OMB and the administration. A lot of them who appear before my committee do take their orders from OMB and the administration. NIH and the various heads of the institutes do not. They talked about total candor both publicly, that is a matter of record, and they said the same things privately. I asked them time and time again, and they will give me their answer, not OMB's answer, not the administration's answer. That is the fact for the record and, indeed, when today's questions were asked as to the accuracy of funding and response is given, the same response is given to me behind closed doors when we met with each other ahead of time.

In your prepared statement, you state, for example, that AIDS funding the NIH is actually not new money but reprogrammed funds, and I want to make plain that is incorrect. I am not here, as I say, to contest your science but I would like to set the record straight, we did not reprogram or reshuffle any programs for AIDS either in fiscal year 1985 or in fiscal year 1986. That is all new money.

Now, it could very well be you could say that is inadequate money. I don't know how else except through the hearing process that I am supposed to make that ascertainment, but I know this, that statement had best be stricken because that is new money.

I go on to say adequate funds are simply not available to attract the best minds in our country to the problem of AIDS. Would you give me, since this is an appropriations hearing, what funding you would consider to be adequate?

Dr. HASELTINE. In response to your remarks, the first thing I would say is that the impression I gave that there is not adequate funding for vaccine, for therapy or fundamental research I stand by. I have seen what goes on, what is going on, and I believe that there is a very serious need for more funds.

For that, I don't blame anybody here, not this committee, not the people in the Government. What is emerging is a very rapid picture of a disease that is spreading beyond what we expected it to do. And given the contacts that people were operating in 1 year ago, 6 months ago, the best and most reasonable decisions were made. I would say given the context today where we realize the potential for the spread to the heterosexual population, the number of women currently infected, the seriousness of the disease and the fact it may be an irrevocable brain disease, not only immune system disease, we have a much, much bigger problem than we thought we had.

For that reason, the only reason, not the intent of this committee nor the people in the Government, I would say we need more funding.

Senator WEICKER. Let me address that statement if I might, just to explore it for a minute. There is no question that as the research is developed and new matters come to the attention of the medical scientific community, additional funding has been requested. That is an ongoing basis. No better example than that is $61 million in 1984; $104 million in 1985; $126 million in 1986.

We know of the additional money, $70 million, which was mentioned here today by Dr. Mason. I would expect beyond that before the year is up there will be additional funds, for specific purposes—for specific purposes.

I want the record to be clear this has been tracked very carefully, and I might add in a precise way, just as you have to be precise, so does the preparations process have to be precise.

Nobody has had to wait around for fiscal year budget hearings. This has been instantaneous as the determination has been made by the scientific community, not by the politicians—God Almighty, you go ahead and let the politicians take a hold of this thing, Dr. Haseltine, and you will have $1 billion out there floating around. All I can do is try to make this a nonpolitical effort and get the best scientific minds to instruct me as to what is needed. That has happened.

If, indeed—and again, I come off a track record, as you well know, of having fought tooth and nail and expended a great deal of political capital in the area of grants, for example, and many others. I am not afraid to fight, but when I get my advice from the scientific community as to what is needed, I am not going to argue against that.

I will add on my own political Kentucky windage, if you will, in terms of what is needed in terms of dollars.

What funding would you consider adequate to the occasion?

Dr. HASELTINE. I submitted, or will submit along with my testimony what I call a battle plan. That called for funding in additional fundamental research of $30 million. An additional $30 million for vaccine development and additional $50 million for clinical trials. I think the funding levels for public education and for epidemiology have been adequate. Those are numbers I arrived at after discussion with a number of my colleagues at Harvard and the Boston medical community.

Senator WEICKER. An additional $50 million for clinical trials. Two questions there.

No. 1, did you arrive at that figure before you heard the additional $70 million request?

Dr. HASELTINE. That is correct, before. I was very gratified to see—as I listened to the testimony, I haven't seen their request, it was two components. One was for clinical trials and the other was for public education, a breakdown of 50–20. I think that is a good program. I think the vaccine program is substantially new infusion of funds over and above the $26 million requested by the Secretary.

In there, if you are going to make a vaccine, I think in this case, we have a very difficult job ahead of us to make a vaccine. You heard if you immunize people they will die faster. That is a real possibility because the immune reaction might be part of this disease. That is a big problem in itself.

Also, this virus lives inside of cells, travels from cell to cell without ever getting outside where the immune system can see it. That is a big problem. We think it may be necessary to stop the very first virus infection.

We have big problems with many vaccines, that is not even mentioning the fact that virus may change so fast that the vaccine cannot keep up with it. Contrast that with the new money transferred from public health programs designed for vaccine development.

The amount of $150,000 to study the outside virus. That is virtually ignoring the problem; $1 million for testing and evaluation of vaccine. That is the administration's request which is virtually ignoring that problem. We need a lot of money. We need chimpanzees, very expensive. We need to develop the very basis for doing the vaccine which is infecting an animal in the first place, and we are barely sure we have that with some chimpanzees and not other animals. There are just not that many chimps we can get our hands on to do our studies.

We better find other animals. Those are big expensive programs; $150,000 and $1 million doesn't barely begin.

With respect to how much money is new and how much isn't new, you said you were spending $108 million this year, $100 million—somehow in some figures I have seen comes up to a $40 million increase.

I don't compute it that way, $108 plus $126 doesn't mean $46 million. Somebody knocked down the budget coming in to get more money. I am not an expert on money, as you pointed out. I realize fully. Those numbers don't seem to me to be a $40 million increase. And if you look at Secretary Heckler's budgets as to where the new money was coming from, it was rebudgeting within the Public Health Service. There was money taken away from the National Cancer Institute construction program to be put into AIDS. There was money taken from some AIDS projects to be put back into other AIDS projects. That is rebudgeting.

Senator WEICKER. I will be glad to make staff available because I do take certain pride in the integrity in the work of this committee. When I saw new money, period. There are too many times I have to confront the administration when they do try to reprogram and when they do reshuffle money, nobody enjoys nailing them out there better than I do. In this case, the answer is no, they didn't. We are talking about new money. Again, you and I would be on the same side of the argument quite frankly as to what the money should go to. To me you can take the money allocated to science, medical research, and take the money of defense and totally reverse it. I want to be clear to you and the public, the scientific sides, I don't dispute that. I am not one to rule on that.

Monetarily they should know that this is new money, that it has been directed to AIDS. It could well be by your testimony here today I will once again review the vaccination program and we might need some additional funds there. I have no dispute there. It appears on the matter of the clinical trials and drugs, that might be coming somewhat to the level you want anyway. I just want to make this clear, what upsets me I suppose on the funding area is one of the reasons why this hearing was born, one of the leading publications in my area of the country, a large editorial in effect saying the Federal Government hasn't done anything in the area of AIDS.

I sat there and read this, a very knowledgeable publication, one close to me, I might add. I couldn't believe what I read. They were making a misstatement of fact in an editorial. Or in the AIDS concert which took place the other day, somebody told me one of the entertainers stood up there and said we are going to raise $1 million here and, look, the Federal Government hasn't done anything. That is a misstatement of fact to the American people. I don't want to compound that, if you will.

You have every right, and I might add, I have every respect for you and I mean that sincerely, to say we ought to have more or redirect it here, and that is what this hearing is all about. I don't want to give you the impression the Federal Government is sitting back doing nothing. There is too much dedication and too much money involved in this effort and has been for the last several years. Do you have any specific drugs you would like to see clinically tested not on the list I know about?

Dr. HASELTINE. On that issue I will defer to people in the National Institutes of Health, National Cancer Institute and I would do exactly what you have done, ask them as to what drugs should be taken. If you ask me do I have specific areas of fundamental research or specific areas where I would like to see vaccine development go forward, I certainly do and I can provide that to you.

Senator WEICKER. I gather you work with the National Cancer Institute.

Dr. HASELTINE. I certainly do and they have supported me and continue to do. I work closely with many of the members now.

Senator WEICKER. They have knowledge of what you feel?

Dr. HASELTINE. Absolutely.

Senator WEICKER. Good.

Dr. HASELTINE. What I would say is, again, the alarm you heard me express I think is heartfelt alarm. I think of the magnitude of this problem. It is concern that our best minds aren't yet fully mobilized. None of the scientists you will meet who are really good scientists needed AIDS any more than any of us needed AIDS. We have more problems to work on than we can work on. This is the golden age for biologists. There is gold everywhere we look. Why work on AIDS? How do you get those people to work on AIDS? You can't just say do it because you should. You have got to provide something so they can do it. That is what I am arguing for.

Senator WEICKER. One last point before Senator D'Amato asks his questions. Do you have documentation in any way for these Army studies or the matters which yov refer to? Do you have documentation, in other words, to back up your conclusion as to what is going on?

Dr. HASELTINE. I have the direct confirmations with people in the U.S. Army, Walter Reed Medical Institute, as to the validity of those numbers. I obtained those as an investigative reporter would. They are not my own research. I want to emphasize that. Those are not numbers I generated. Those are numbers I had repeated to me. I asked if I could use those numbers. I was told I could and I am willing to provide the information where the information can be obtained.

Senator WEICKER. I appreciate it.

Senator D'AMATO. Thank you, Mr. Chairman.

Doctor, let me not take issue with you. I don't think you are going to take issue with my statement. One of the things that you indicated was that we may not stop the spread of the disease through communications. I think given the fact we are going to have to wait until science can, hopefully, develop a vaccine to deal with this virus, that communication is probably our best method in the meantime. We must communicate to the people very clearly what the risk factors are, the seriousness of this disease. We must communicate the fact that we are talking about not just a life-threatening disease, but as a limited body of research indicates, the proportions and magnitude of what we mean by life-threatening.

There is no one we know of that has been cured of AIDS. Let me also say that when we talk about cigarettes and the danger of smoking, that is a little different. A recent limited study done at Columbia, which was just revealed in the New York Times surveyed 700 homosexuals. They went into detail on 100. This survey indicated that the sexual activity of these homosexuals prior to the AIDS epidemic, or before the time when AIDS became well known, included approximately 64 sexual encounters with different people in the course of 1 year. That is just incredible. You know that this is the average. Obviously, within this group there are some who have had more than 64 partners, considerably more, maybe 100 plus and more. These figures may be on the low side.

This same study indicated that after the information regarding AIDS had been disseminated, the deadliness and the manner in which this virus is spread, the sexual activity of those within this same group with different people during the course of 1 year dropped to something like 16 or 18. This is substantially down.

I don't think, therefore, that we should minimize the effect of what getting the correct information to people can and will have, particularly to segments of our society who should be careful.

You mentioned that one out of five prostitutes in the city of New York may be carriers. There is a very real chance of this being communicated. I think people are entitled to that information. We should give it to them. We should dispel ignorance and fear with facts. We should make people conscious of what the reality of these situations is. I think it is terribly important.

Second, let me say this to you. You mentioned that 1 million may be infected. How did you arrive at this figure. Are you talking about 1 million that tested positive? What are the strengths and weaknesses of the blood test? You mentioned that. What does that 1 million represent? How do you view the 1 million Americans who are infected or affected?

Dr. HASELTINE. Senator, let me address your last question first, what does 1 million mean. It means if you test for the presence of antibodies, they would be positive. There is a positive antibody test meaning you carry the virus. To the best of our knowledge, it comes both from—to isolate viruses from all types of people, whether healthy or sick, who are antibody positive. In those cases, it appears you can usually, if you are a good virologist, isolate the virus from virtually every person who is positive. First of all, the very nature of this virus——

Senator D'AMATO. Doctor, right at that point, you are saying that 1 million, if tested positive, have the antibody. What we are really saying is at some point in time, you will have contracted AIDS.

Dr. HASELTINE. Nobody can say that. All we can say is we have followed the disease for a period of 6 to 7 years now and in that time, a substantial, I mean truly substantial number of people have contracted serious symptoms.

Senator D'AMATO. What percentage?

Dr. HASELTINE. It depends on the study. In a 2-year followup in Boston, that number was 25 percent in 2 years. That is a small number. The people here sitting behind me from the Centers for Disease Control can give you much more accurate numbers based on larger studies. You have to realize the dynamics of this. The virus gets into the body and works its effect extremely slowly. We have only followed it for 6 or 7 years.

The number of people infected is rising extremely quickly. Only those people who get sick at the very first part of the distribution show up early. So if you take total number of sick to total number infected, you get 5 to 10 percent. If you take how many people get sick, follow year one and year seven, in some studies it is 30 percent who have AIDS, 50 percent who have some other serious illness.

Senator D'AMATO. Connected with AIDS?

Dr. HASELTINE. AIDS in some sense. Thirty percent after 7 years.

Senator D'AMATO. And 50 percent in addition with other serious diseases?

Dr. HASELTINE. Total of 50 percent with other serious diseases. However, we don't have full measure of this virus. I think there will be a good argument to make what is going on in the brain occur more slowly than what goes on in other parts of the body. We may be really only looking at the begining of what the brain disease is going to be.

With respect to another question, how good is the blood test? The answer to that is extremely good as a screening, as you have heard testimony here. However, there are certain people it cannot and will not detect. So no matter how good it is as a screen, there are still people who will slip through and they will slip through because they are just entering a state when they become infected. We have that problem with hepatitis.

We can guess how big that number will be, and it will be finite. There will be people even after the test is perfectly administered, they will slip in.

There is another group which is also troublesome. For some reason some people infected with this virus never make an antibody response. It is something new to science. We don't understand it. But it is true. You can find people who don't have antibodies, even though you get virus from them. How in the world would you ever find those people? Well, people said maybe such people exist, they look at the sex partners who have AIDS, maybe routinely isolate virus from but never found any antibodies, and they followed those people and still can isolate virus but no antibodies. That is a whole new system, although the system is as good as it can be and administered absolutely. There is potential for the problem.

Also, there is a problem of false positives, as was referred to. This is good for screening but not definitely for diagnoses. There is a problem, if you use only this test, you will inform people they may be infected and create a lot of psychological harm without a basis.

Senator D'Amato. Let's go right to that point, but first let me commend Senator Weicker once again for calling this hearing so we can begin to focus in on what has been done, what is being done, what the problem is, and what the facts are about AIDS. Certainly his efforts to see to it there are sufficient funds are commendable. These efforts certainly will receive this Senator's support, and the support of all of the Members of the Senate and of the Congress and of the administration.

Having said that, how do we deal with the problem while scientists are grappling with the cure? The prevention of it is very important. Should we tell people who have been identified, given the fact that there is a very real possibility or probability, if they test positive with these antibodies, that they are going to come down with this disease or other diseases that come about as a result of this virus; we don't tell them?

Dr. Haseltine. You are dealing with a man who spent most of his life in the laboratory and not in the halls of the public.

Senator D'Amato. Shouldn't we test every U.S. soldier, everyone in the military?

Dr. Haseltine. Let me give you my opinion on the first question. That is I think those people infected might want to know they might infect the people they love the most. I think, in my opinion, it would be a reasonable decision to inform those people. But you should realize, this is a screening test, not absolute diagnosis. There are better ways now of followup tests. They are extremely expensive.

Senator D'Amato. They could then proceed to take other tests?

Dr. Haseltine. That's right. It would cause some temporary anxiety. I think there is need for more development tests. That is the good news on the horizon. I believe within 1 year there will be commercially available much more tests. I know there will be very specific tests that alleviate both that screening problem and diagnosis problem. There won't be a test for some time to tell whether you have a virus and no antibodies. That is a technical problem we haven't solved yet.

Senator D'Amato. What about the military?

Dr. Haseltine. I think they should speak for themselves.

Senator D'Amato. Maybe we will have a hearing with respect to that. Thank you, doctor. Thank you.

Senator WEICKER: One last question before we move on to our next witness, Dr. Malcolm Moore.

I have with me here a member of the Defense Subcommittee staff. The question raised is are you referring to the Berlin study that represented a size sample of 74?

Dr. HASELTINE. I don't know what the size sample was. It was a study completed in June 1985. Also, there is a number from Fort Bragg of 2,984 in which 1.5 percent of the Fort Bragg soldiers were infected.

Senator WEICKER. I think it should be made clear the study will be made available, but apparently this was a study of a sample size of 74 persons of whom 4 people showed up positive. That is out of the military population of 320,000. I am not a pollster or statistician. I don't think that is something I would like to arrive at a conclusion on in the sense of a bottom line.

Dr. HASELTINE. The fact that our soldiers are being infected by prostitutes in West Germany, I think, is clear. How big a problem that is going to be depends upon how many of our soldiers use those infected prostitutes. The time factor over which that was taken was 4 out of 74 people so I see it pretty high as people who report to be infected.

Senator WEICKER. I thank you very much for your testimony. Let me say, I think it is terribly important that we have an active debate, if you will, on these issues. It assists the committee, if you will, in arriving at its conclusions. Thank you for taking the time to testify before us.

Our next witness is Dr. Malcolm A.S. Moore of the Memorial Sloan-Kettering Cancer Center.

STATEMENT OF DR. MALCOLM MOORE

Dr. MOORE. Mr. Chairman, as an active member of the biomedical research community, I wish to address a number of issues in relationship to what we have termed the AIDS crisis from the perspective of a research investigator who has participated in some aspects of AIDS but primarily I consider myself an immunologist and hematologist, so I speak from the outside of the problem, as it were, and discuss how biomedical research resources have been applied to AIDS, how I will see the impact of additional funding and what sort of resources we might have available and need.

I think it is critical to determine if the nature and extent of Federal support for biomedical science has enabled us to cope rapidly enough with the problem of AIDS and whether the infusion of additional money for redistribution would have a significant impact on the development of a cure for the disease.

Certainly the allocation of Federal resources to fundamental biomedical science by world standing can be construed as having been generous. Although warning signs are being raised about the insecurity or instability and its gradual erosion by inflation and other causes.

Thus, our national research and clinical base which must be maintained, indeed, must be expanded significantly in order to be flexible enough to cope with the future health crisis of AIDS and on down to the future of the crisis we will experience during the course of the rest of this century.

However, I would like to place in perspective the problem, as did Dr. Ludwik Gross in his overview of a major symposium on HTLV virus in AIDS held at the NIH less than 1 year ago in which he pointed out that in a total population of 230 million, we can anticipate 870,000 cases of malignant tumors each year alone, including 63,000 new cases of leukemia and other malignant diseases of blood-forming tissue. All of these are, of course, equally life-threatening. We have been informed that the incidence of AIDS, the number of cases reported to date is in excess of 13,000, and the rates among single, never-married men 15 years or older is approximately 200 per 100,000 population in such high-risk areas as Manhattan and San Francisco, with a 2-year mortality rate exceeding 85 percent.

Obviously, we do not want to diminish how drastic this problem is and how rapidly it has come upon us. I was very pleased to hear that there was not going to be any question of redistribution of money from other sources. I certainly do not wish to observe a situation where we rob Peter to pay Paul. I certainly thank the Senator and this committee for achieving that.

Through its geographical location in New York and the high incidence of malignancies, such as Kaposi's sarcoma and lymphomas associated with AIDS, a large number of patients with this disease have been seen and treated at the Memorial Sloan-Kettering Cancer Center since the disease was first reported. Indeed, we are probably seeing about 5 to 10 percent of early cases in the initiation of this discovery. We also were observing the first cases of pediatric AIDS as part of our program in treating severe immunodeficiency, generally a genetic defect, in newborn babies. We started to see increasing numbers of such cases, and these subsequently turned out to be babies who have been infected with the AIDS virus in utero. And the course of treatment has generally involved bone marrow transplantation.

Obviously, such a burden is difficult to sustain by any single institute, and the clinical care and management of patients with AIDS and, in particular, the initiation of large-scale controlled phase II trials of antiviral and immunostimulation therapy with various lymphokines should be undertaken as a collaborative effort initially among what I would term tertiary care centers with the expertise in the handling of patients with opportunistic infections and associated malignancies.

We have the infrastructure with our comprehensive cancer centers, and most of these centers are, in fact, involved in the care of its patients. As Dr. Haseltine pointed out, the geographical distribution and proportionality among the different centers is definitely uneven.

I think in dealing with the past and future support mechanism for AIDS research both, basic and clinical, I think the following points should be made. The outstanding progress in the identification, isolation, and characterization of the causative agent of AIDS and its mode of transmission was supported by Federal funding generally for very basic studies in molecular biology, virology and epidemiology, but it should not be forgotten that major breakthroughs evolved from the funding of the Cancer Research Program in the course of a search for human cancer or leukemia-producing viruses.

The scientific nature is an inquisitive one and as observations, frequently serendipitous, are made even in a highly focused program such as the search for human tumor virus, the flexibility of our current system is highly desirable and has allowed the identification of the various viruses and parameters associated with IADS and also the discovery of the growth factor for normal T-lymphocytes. This T-cell growth factor, all Interleukin–2, proved critical for normal T-cell growth and has greatly assisted in the isolation of the AIDS virus and has probable value in AIDS therapy.

Research activities among colleagues and myself where we concentrated on an understanding of the origin of the T-lymphocytes and that derivation from early cells in blood-forming tissue. This basic research was supported by various conventional R–01 program project mechanisms of Federal support. We were successful in the purification of such Interleukin–2.

In our preclinical studies that were confirmed and extended in many other labs showed lymphocytes of patients with AIDS are defective in production of this growth factor.

Furthermore, it was possible to demonstrate that the impairment of the growth of the lymphocytes of these patients, particulary when stimulated by the use of various monoclonal antibodies, this defect could be reversed in vitro by this naturally occuring human substance. The logic, therefore, would be to move into clinical trials to treat patients with AIDS with this substance which they fail to produce in adequate quantities.

We have initiated and completed a number of phase I and phase II trials to determine toxicity, to determine whether there was indeed any effect.

The information we gained has been invaluable; however, it was not effective in reversing the AIDS process, and the reason is presumably that the very cells that are stimulated by the substance are then reinfected by the persisting AIDS virus and in process of infection are destroyed, and so we feel that the most efficacious protocols, as have already been discussed, would involve procedures that interfere with the replication of the AIDS virus, for example, suramin, which is being discussed, an antiprotozoan drug and various nucleoside analogues.

The toxicity of these agents, and their failure to lead to direct recovery of T-cell function, suggests that future clinical trials should involve combinations of agents with antiviral properties and immunostimulatory features, and such clinical trials are planned at our institution.

In addition, other naturally occurring biological response modifiers have been explored. The interferons, some significant regressions of the Kaposi's sarcoma have been reported with interferon alpha, for example. And I feel this combination biotherapy may usefully be expended by the inclusion of other naturally occurring products of T-cells and their activation.

We know T-cells that are defective in AIDS produce up to 20 different molecules, lymphokines, that influence the function of a number of different host defense cells against bacteria, cancer, and other opportunistic infections. It is the availability of these naturally occurring lymphokines in large quantities as the result of dramatic recent progress in recombinant DNA technology that has made available such substances in sufficient quantities for clinical trial. So I think we have prospects here of introducing some of the products of T-cells if we are, indeed, unable to restore totally a function of the normal T-cells of these patients, we can perhaps substitute many of their responses.

The mechanisms developed by the National Cancer Institute over the years for clinical trials of conventional chemotherapeutic agents and more recently the guidelines proposed by the biological response modifier decision network committee, provide a clear blueprint for comparable clinical trials organizations in AIDS with phase I–A study to determine toxicity and phase I–B to closely monitor parameters readily measurable as indicators of response, such as restoration of T-lymphocyte functions and changes in viral titer.

Rapid progression to phase II trials in relatively small groups of patients in a limited number of specialized centers could then be followed by extensive cooperative or regional collaborative trials, with the emphasis on rapid accumulation of information by accumulation of large patient groups in controlled trials, preferably under some kind of overall supervision or coordination.

We are not going to cure AIDS by simple expedient indiscriminately throwing money at it. The temptation to increase the number of scientists and clinicians participating in AIDS research by any simplistic expedient, such as being excessively lenient in the fundable priority scores established by peer review study sections in grants focused on AIDS, would attack the validity and importance of peer review and the success it already has had in such supporting innovative research currently underway in AIDS. I would like to see the peer review process accelerated. I would like to see it expanded.

I think there is a time factor here that is proving a problem.

The introduction of greater numbers of people working on AIDS and the introduction of fundable proposals of dubious merit undertaken by investigators with limited qualifications in unfavorable environments must be prevented at all costs. This is counterproductive. We cannot assume just sure chance is going to lead through the breakthrough, if the chance occurs in any environment where it cannot be recognized or capitalized upon.

I would abbreviate my comments in the interest of time. I would think we certainly should elect in the distribution of this funding to go with quality over quantity. Certainly serendipity has played a crucial role in new medical advances, but again usually only in the context of either highly qualified scientists and/or research environments capable of recognizing and capitalizing upon such chance observations. As a former member of the NIH study section reviewing a broad range of immunological grant proposals and as an informed outsider in the AIDS area, enough promising leads appear to exist already, and funding should be focused on the rapid expansion of these current endeavors, particularly clinical trials, so that we can focus more rapidly upon the most therapeutically attractive options.

Mandatory information exchange between federally supported investigators should be strengthened and some form of oversight committee or individual should be formalized so that the federally sponsored effort speaks with one voice to the public and the patients and will act as a central repository of all information on the disease.

Misinformation, distortion, and misunderstandings abound, as do false expectations. The public should be made to understand the dramatic developments that have taken place in understanding AIDS, perhaps one of the greatest feats in medical science of this century, but the public must be better informed on these various controversial issues, such as communicability, time constraints, and complexities of bringing new drugs or therapies to general clinical use.

I think Senator D'Amato's comments and proposals are very relevant to this.

In looking at the quality and numbers of biomedical investigators trained in the various disciplines necessary to undertake the task of AIDS and in the clinical basic research, it is fortunate that federally supported postdoctoral and clinical training programs have in general provided the qualified individuals needed to tackle the AIDS crisis. The importance of continuity of such training must not be overlooked. I would like to feel that such individuals are going to be attracted to an involvement in AIDS research. I went through my own figures over the last 10 years and of the approximately 90 basic research postdoctoral and clinical research fellows through my program in that time, approximately 20 percent of them are now actively engaged not just in our own institute but others on projects that are directly relevant to the AIDS Program. That is the end of my testimony.

Senator WEICKER. Thank you very much, Dr. Moore. One very brief question. Am I given to believe from what you said, Sloan-Kettering itself, in other words, is involved in research outside, in other words, that is connected with the Government?

Dr. MOORE. Outside?

Senator WEICKER. Outside that research which emanates from the Government, Sloan-Kettering has embarked on its own effort in this area?

Dr. MOORE. Essentially Sloan-Kettering is a comprehensive cancer center and has a program support from the National Cancer Institute and the majority of its funding from research and clinical basic research comes via the conventional federally supported mechanisms of program projects and R–01's in individually initiated research.

Senator WEICKER. Can Sloan-Kettering initiate research in these areas or do you have to await direction from NIH?

Dr. MOORE. We have always made it a policy to await direction from NIH in this regard. I think this is very important. I would like perhaps to enter into the record my fears that other agencies, particularly the large amount of private money that is being raised, outside any kind of Federal support and supervision, its allocation may take place without the necessary peer review that is always applied to the expenditure of federally supported programs. In other words, qualified scientists and clinicians who are knowledgeable in the AIDS area should be involved in the private expenditure of money as well as in the public sector.

Senator WEICKER. In other words, whether it is Harvard, Sloan-Kettering, whatever, the public should be qualified better to go in those directions than some individual who might be raising funds for AIDS without any knowledge as to how that money is going to be used.

Dr. MOORE. As you well know people, the people most successfully raising funds are not necessarily the ones most knowledgeable about the diseases they are raising those funds for.

Senator WEICKER. Senator D'Amato?

Senator D'AMATO. Mr. Chairman, in the interest of time, I am going to forego my questions but I am going to say to you, doctor, that you don't have any argument from either Senator Weicker or myself regarding the quality/quantity issue. We will see to it that the resources we do have are put into those areas where we are going to get the kind of quality research and control that will most probably give us the answers to this perplexing question of AIDS.

Senator WEICKER. I just want to say one thing to Dr. Des Jarlais. I had to remind myself, Dr. Haseltine, as to your slight of my alma mater, Yale. I said to myself, consider the source. [Laughter.]

I didn't want to let that pass by. I am not going to have a Harvard man come here and do a tap dance on Yale without some sort of response. [Laughter.]

STATEMENT OF DR. DON DES JARLAIS

Dr. DES JARLAIS. I would like to thank this committee for this opportunity to testify, particularly since I have been conducting research on the intravenous drug users. This group is the second largest risk group and it probably receives disproportionately less attention than some of the other groups at increased risk for AIDS.

Of the current 13,216 adult cases of AIDS reported to the CDC, 3,393 have involved drug use at some level; 1,144 of those involved gay men who are also injecting drugs. The CDC classification scheme puts all gay IV drug users into the gay men risk category; therefore, it tends to symptomatically underrepresent the amount of drug use involved in the transmission of AIDS.

In addition, the IV drug use group is the primary link to two other groups at increased risk to AIDS, heterosexual partners and children. Of the 133 cases where heterosexual transmission appears to be the route of transmission for AIDS in the United States, 97, almost 73 percent have involved transmission from an IV drug user. Of the 186 children who have developed AIDS in the United States, 98 or 53 percent are children of an IV drug user. Clearly we have not been able to control the epidemic in the United States without specific attention to the IV drug use group.

I also would like to note it is fitting for an Appropriations Committee to hold these hearings. We have had various discussion of the appropriate amount of money for research on AIDS. I would merely like to make a point if we do not spend the money on research in the area of AIDS, we are going to spend much larger amounts of money for the treatment of AIDS cases. The best estimate for the treatment of the drug user with AIDS is about $150,000 per case. This is slightly higher for gay men because of the more serious complications and more intensive care unit required for IV drug users.

In New York City, we are currently having two cases per day in IV drug users. So that is roughly $300,000 per day being spent on medical treatment for IV drug users in New York City or roughly $900 million per year.

As the drug use group continues to grow, we are talking about very, very large expenditures of medical resources for mere treatment of AIDS which at present does little other than alleviate some of the symptoms and certainly does not cure the disease.

I will briefly review some of the research that we have been doing in drug users. Before doing that, I would like to specifically acknowledge my colleagues at Beth Israel Medical Center, Narcotics Drug Research, Inc., Manhattan Veterans Administration Hospital in New York, University Medical Center. AIDS truly does require interdisciplinary research. It is not the type of thing one speciality is sufficient in conducting research. I also would like to specifically thank the National Institute on Drug Abuse which has provided funding for this research.

We have been studying the epidemiology of the HTLV-III virus in drug users in New York and elsewhere. Our data from 1984 shows that approximately 60 percent of IV drug users in New York City had antibodies to the virus.

Senator D'AMATO. Doctor, if I might, in 1984, you had a study which indicated that 60 percent—60 percent of the IV users had the antibodies?

Dr. DES JARLAIS. Yes; and presumably also are carrying the virus.

Senator D'AMATO. Well, I want to tell you how unfortunate the media took off, but if that isn't reason for those who are using drugs, again they ought to take a look and wake up. Sixty percent in 1984 tested positively for the antibodies. Those are intravenous drug users.

Dr. DES JARLAIS. Those were people injecting drugs. They did not apply to people just taking drugs through other means of administration.

Dr. HASELTINE. Could I comment on that?

Senator D'AMATO. I don't think people have the slightest idea.

Dr. HASELTINE. I don't think they do. Numbers really are staggering. If you look in the Manhattan New York area today, 60 to 80 percent of drug users are infected. Jersey City, 50 percent. Atlantic City, 5 percent. San Francisco, 50 percent drug users. It is not too late to stop it.

Senator D'AMATO. It is not?

Dr. HASELTINE. It is not too late to stop it outside of New York City. Boston is 12 to 20 percent infected. Those are high rates, but they are going to be 100 percent except for those who use new needles. There are 1 million drug abusers or more in this country. A lot of those—that is the point I was making before, about how serious this threat is to every simple human being in this country.

Dr. DES JARLAIS. We also collaborated with other research institutes in San Francisco and Chicago where both those cities are showing approximately 10 percent antibody positive for blood collecting in 1984 and 1985. We are also starting collaborating with researchers in Western Europe and the general findings from Stockholm down to Valencia show a range of approximately 20 percent, as high as 30 percent in Zurich, reports as high as 60 percent, although those are very preliminary, in Valencia. About 25 percent in Denmark. Clearly this is not just a U.S. problem, it is a Western European problem and there is also the potential for the virus spreading to drug users in underdeveloped countries where the medical resources for both treatment and prevention of the disease are probably considerably less.

We have also conducted historical research. We have blood samples collected from IV drug users going back to the middle 1960's. Those were frozen and put away for future research. In analyzing those historical samples, we find 1979 seems to be the big breakthrough in terms of antibody presence. We found 30 percent of our 1979 samples of IV drug users in Manhattan had antibody of the virus. This rose to approximately 40 percent in 1980 samples. Approximately 50 percent in 1982 samples and approximately 60 percent in 1984 studies. So we have a relatively good idea of the rate of spread certainly in Manhattan. Approximately 5 percent per year. This does mean that there are good opportunities for prevention efforts; That even in New York with approximately 60 percent now, there are still 40 percent unexposed and the spread is relatively moderate. It is really not as fast as hepatitis-B will spread through a drug use population and prevention activities throughout the country certainly are justified.

Senator D'AMATO. Are you saying people who have sexual relationships with those who are drug addicts are substantially at risk, men and women?

Dr. DES JARLAIS. Women are certainly substantially at risk.

Senator D'AMATO. If 60 percent test positive——

Dr. DES JARLAIS. Sixty percent of the drug users.

Senator D'AMATO. Test positive.

Dr. DES JARLAIS. Correct.

Senator D'AMATO. And those people who have sexual relations with drug addicts are substantially at risk, aren't they?

Dr. DES JARLAIS. They certainly are. They certainly should be taking what are called the safe sex precautions if they are going to have sex with IV drug users. They should attempt to limit the number of partners they have.

Senator D'AMATO. They better make sure the partner doesn't carry it. One of the ways—if 60 percent, again, of the addicts are carrying it, that is the average, it would seem to me the natural conclusion is if you have a relation with a person who is an addict, at the very least, you better get a test to see whether or not they are a carrier. It is a pretty good chance they are a carrier and you are at risk.

Dr. DES JARLAIS. There certainly is. I would like to point out there are great psychological difficulties in going into a marital relationship where one partner is a drug user or——

Senator D'AMATO. At least let the people know the facts. That is why it is so important this hearing be today. We don't want to start a thing. Again, I think it is important these facts be known.

Dr. DES JARLAIS. I agree completely.

Senator WEICKER. I think the point Senator D'Amato makes, the information has to be repeated. It is the point you made at the outset of the testimony which is I'd say in the minds of most Americans, this is principally a problem among the gay community of the United States. Well, it is clear it is not. It is a problem, in the area you have described, for drug users. That certainly includes heterosexuals, men, women, and the whole spectrum of our society.

Dr. DES JARLAIS. It certainly does.

Senator WEICKER. I might add, it also raises the question from an appropriations point of view as to whether or not—that is a vote, we have to leave here for a few minutes. I wonder if you would answer this one question. We really have focused most of our attention on the area outside your area of concern. Could you address yourself to the funding levels as they apply to this aspect of the problem?

Dr. DES JARLAIS. I have submitted written testimony, so I will specifically address what I see is needed for increased funding. I think there is a great need for increased research funding with transmission among IV drug users. We have considerable evidence showing educating drug users does lead to changes. If you reduce the needle sharing, but there are constraints on that risk reduction, we need additional research that goes beyond merely providing education. That we are really ready for a second stage of prevention research, what is needed beyond just telling people. Unfortunately people are not totally rational about their health-related behavior. We need to find ways to go beyond just educating them.

Senator WEICKER. The ADAMHA funding has traditionally been the lowest of funding within the category. Can you just briefly address that as to whether it is something—you are obviously associated with that in the sense of your relationships?

Dr. DES JARLAIS. Yes.

Senator WEICKER. Do you feel more is specifically needed by that agency?

Dr. DES JARLAIS. Oh, a great deal more is needed, and I would point to a couple of particular areas. There is need for additional research on how to prevent people from starting to inject drugs. Clearly telling them about AIDS will have some effect, but if telling people that injecting drugs is bad for you was sufficient to keep people from injecting drugs, we wouldn't have the problem we have to start with.

I would also like to make a specific mention of research and the public reactions to the AIDS crisis.

Senator WEICKER. What you are saying, if I can extrapolate remarks—what was the percentage in New York?

Senator D'AMATO. Sixty percent.

Senator WEICKER. What you are saying now, 60 percent of you who are users will die?

Senator D'AMATO. It will make an impact, believe me.

Dr. DES JARLAIS. It certainly will. From a public health point of view, I think we should be finding ways to go beyond just that impact. We are proposing specific research to look at people who are sniffing heroin and cocaine, thus at very high risk of starting to inject and trying to work out specific intervention programs with that group to prevent them from starting to inject. Clearly they are the most at risk for starting to inject and they are a group where you may be able to make a big impact.

There is a big turnover in the drug use community with a lot of people starting to inject and a lot of people stopping. If you could plug up that front end, you may be able to greatly reduce the total amount of drug use.

Senator WEICKER. In the past as you said you have been able to say to those, you try to steer away from drugs, this would be bad for you. Now you have some very precise figures over here when it comes to the AIDS situation. It is survivability or fatality. They are very unforgiving statistics. They are all very precise. I think we all would agree with that. You can tell this group you are trying to make sure never inject drugs in the first place, you tell them something bad is going to happen, you know something is going to happen.

Dr. DES JARLAIS. Another area is the societal reaction to the AIDS epidemic. There is clearly potential for employment discrimination against IV drug users as a fear of AIDS. Employment is a central aspect of successful treatment, of rehabilitation of IV drug users. If employment discrimination starts on a large scale, we are going to undermine our ability to successfully treat IV drug use. We will then have more drug use, more crime, and more AIDS.

Another aspect of the societal reaction I feel needs to be studied is the amount of panic and hysteria that is occurring in some areas of the country with respect to AIDS. Clearly the actions of keeping students out of school are not productive. We do not have any research ongoing as to how people learn about AIDS, what tends to stimulate excessive fears. What tends to be reassuring, the emotional blocks they have in terms of reading the newspapers and hearing things on TV, how that relates to various actions that may be very counterproductive from a societal standpoint, such as the school strike. And I would also like to point out that the potential for public panic and hysteria, we are really just scratching the surface. Right now the panic and hysteria has focused primarily on people who are already identified as having AIDS. If that panic or hysteria should ever start to focus on the much, much larger number of people who are probably carrying the virus, we have a potential crisis and the credibility of our public health officials, school system, employment discrimination, and a wide range of societal problems that might be minimized or alleviated if we had ongoing research on how people react to hearing information about this.

Senator WEICKER. Thank you very much. I will take your statement in its entirety for the record. And I want to thank—there might be questions which we will submit to you for response to the record, all of you. I want to thank you for taking your day.

I think the other thing, though, that comes out as we get testimony, there are a lot of answered questions. I think we really know what needs to be done, whether it is the scientific community or whether it is the public as a whole. If we do what needs to be done, it isn't the problem that it could be, and that involves everybody. There is not much guesswork. Sixty percent of those people get——

Dr. DES JARLAIS. Sixty percent of drug users have been exposed.

Senator WEICKER. Take the percentage as your survivability of AIDS, 60 percent are going to die.

Dr. DES JARLAIS. I am not sure all people exposed to the virus will die.

Senator WEICKER. Pretty darn close to it.

Senator D'AMATO. They come down with problems that eventually bring about a termination of life. They come up with a bad kidney disease, forms of cancer, and eventually die.

Dr. DES JARLAIS. The overall outlook is certainly bleak.

Senator D'AMATO. Let me ask you this, a broader public policy question. I may or may not be suggesting an answer. Let's take the statistic that 60 percent of those who use IV drugs are carriers. Isn't it frightening when you think of drug use in sectors of the population such as those in the Army and in public schools. We know that drugs are used in high schools, even in preceding grade levels. This drug use involves the use of IV's, isn't that correct?

Dr. DES JARLAIS. Yes.

Senator D'AMATO. Let's start with the fact that there are presently 1 million carriers. What about the 200 million plus others who are not infected? Isn't there a right to protect society? I don't want to create panic, but shouldn't they know there are people at risk. At least those people who are at risk know, so they don't continue to infect, whether it be sexual conduct or sharing of needles. Let's talk about sexual conduct, we are in a day of sexuality. We are now going to get this epidemic increasing and more and more people become carriers or becoming infected. That is really what we are saying to those who are exposed to the virus. You know, you say you don't want to start a panic. I think, Senator Weicker, the genie is out of the bottle. We don't need panic, but we had better begin to develop some rational plan to deal with whether or not you might have to test everyone to determine whether they should know, if they are carriers, if they care about their loved ones, their families, et cetera.

Doesn't society have a right to know?

Dr. DES JARLAIS. Certainly. My personal point of view would be such testing should be voluntary. People should not be forced to take a test.

Senator D'AMATO. I am not going to get into that. There comes a point when you place all of society at risk, where are the rights of the general public?

Dr. HASELTINE. May I make a brief comment?

Senator WEICKER. You can, except we are going to miss this vote. I think we ought to take care of that. I will be glad to come back to you as soon as we make this vote. I know we are going to lick this problem so let's do away with the panic. Forget the panic. I know we are going to lick the problem, I think it is the point Senator D'Amato is making which is such a good one, there is no point asking Dr. Moore, Dr. Haseltine, Dr. Des Jarlais, to put forth their scientific opinion and say to the public, but you laymen can do whatever you want to out there. As I said before, the public is going to have to make its contribution, just as the scientific community will make its contribution. Between the two—as I said, there is no reason for panic, none whatsoever. I know the scientific community will do the job. I know that. But in the meantime, there are certain simple rules of conduct which greatly assist the scientific community in its task and part of that relates to the area you discussed.

Part of it relates to not panicking. Part of it relates to the fact of adequate funding. All the pieces of the puzzle are there and the full picture is going to appear and I think it is going to appear in far shorter time than has ever been the case in medical history. But the public is certainly involved as to their involvement. We will stand in recess for 5 minutes.

[A brief recess was taken.]

STATEMENTS OF:

DR. DANIEL LEICHT, ACTING VICE PRESIDENT FOR MEDICAL AND PROFESSIONAL AFFAIRS, NEW YORK CITY HEALTH AND HOSPITAL CORP.

DR. ALFRED J. KATZ, VICE PRESIDENT FOR RESEARCH, DEVELOPMENT AND MARKETING, AMERICAN RED CROSS, AND FORMER DIRECTOR OF AMERICAN RED CROSS BLOOD SERVICES

PREPARED STATEMENTS

Senator WEICKER. The subcommittee will come to order.

Our final two witnesses are Dr. Daniel Leicht, vice president for the medical and professional affairs, New York City Health and Hospital Corp. We appreciate Dr. Leicht being here in place of New York City Commissioner Sencer. We understand Dr. Sencer today is dealing with another serious aspect of the disease AIDS in the schools and Dr. Leicht is a last minute fill-in. We are very grateful.

I might add, I would hope these hearings would lend some knowledge to the situations in New York and elsewhere which might dispel some of the concerns that Dr. Leicht and Dr. Sencer and others have to deal with, with knowledge, as I said, those in this fight are going to prevail. Unreasoning words or actions just delay the day when, frankly, the problem is put behind us.

Also we have Dr. Alfred Katz, vice president for research, development and marketing, American Red Cross and former director of the American Red Cross Blood Services. I gather Dr. Katz seems to head up that in the State of Connecticut. Glad to have you here. All the testimony in their entirety will be placed in the record.

Please proceed in whatever way you see fit.

[The statements follow:]

STATEMENT OF DR. DANIEL LEICHT

My name is Dr. Daniel Leicht. I am the acting Vice President for Medical and Professional Affairs of the New York City Health and Hospitals Corporation. I am pleased to have the opportunity to participate at this hearing on the AIDS epidemic.

As you may know, over 35 percent of all reported AIDS cases are in New York City. Figures for the last reporting period show 4,531 cases to date in New York City out of a total of 13,062 cases nationwide. In addition, 50 percent of all children with AIDS are treated in New York City. Furthermore, in New York City AIDS has become the leading cause of death among men in their 20's and 30's and the second highest cause of death among women between the ages of 30 and 34. Since AIDS was first recognized nationally by the Centers for Disease Control in 1981, the City of New York has steadily augmented its funding for the enhancement of programs serving those afflicted by AIDS. These programs are aimed at educating the public about the disease, providing appropriate medical and social services to persons with AIDS and conducting epidemiological investigations and surveillance activities to help us better understand the nature of the disease.

The City's response has included millions of dollars spent annually to provide inpatient care at our municipal hospitals; increased staff and beds in inpatient programs and expanded outpatient programs; increased home care and home attendant services to AIDS victims living at home; expanded outreach programs to the voluntary hospital sector; and developed proposals for scattered-site and congregate housing for AIDS victims who no longer have a place to live. In addition, the City has established ten interdisciplinary health care teams in eight hospitals to provide routine and special medical and psychiatric consultation for all inpatients and to coordinate case management with primary providers in post-acute care settings. The City has expanded public education programs; opened an ambulatory care clinic to address the concerns of the "worried well"; and conducted comprehensive epidemiological studies and case surveillance programs.

I represent the New York City Health and Hospitals Corporation (HHC), the largest municipal hospital system in the country. HHC plays a crucial role in addressing the special health care needs of the AIDS population since almost forty percent of all AIDS beds in the City of New York are in HHC facilities. Our hospitals guarantee to all patients the right to quality health care in an atmosphere of human dignity regardless of ability to pay. The AIDS epidemic has placed a tremendous burden on our human, economic, medical and technological resources. This burden can only be expected to increase as the incidence of AIDS continues its dramatic rise. In spite of this alarming increase in cases, growing public concern and encouraging scientific discoveries, no comprehensive and coherent federal strategy on AIDS has emerged.

AIDS clearly represents a national public health emergency. Although some localities are affected more than others, AIDS is a national problem distinguished from other catastrophic illnesses by a number of factors. There is no definitive diagnostic test for the disease and no known cure. AIDS is a terminal disease. The progressively debilitating course of the illness results in the need for intensive medical and social services.

Over 400 AIDS patients were admitted to our 11 acute care facilities last month alone, a significant increase over prior months. Our average daily census for AIDS is roughly 250 patients corporate-wide. I would like to focus on some of the direct service delivery issues that are specific to the Corporation in treating AIDS patients.

The cost of caring for AIDS patients is extremely high. This is attributable to a number of factors: successive admissions throughout the course of the illness; long lengths of stay due to severe medical complications; more intensive nursing care; higher levels of pharmaceuticals and supplies, often involving expensive and some experimental anti-cancer drugs; and the need for more frequent use of specialized equipment including dialysis units, all of which must undergo special sterilization procedures before they can be re-used.

HHC has a particularly costly case mix of AIDS patients. We are currently treating a disproportionate share of cases from the drug abusing community who usually are sicker with more complications. Over the years these cases have grown to represent a majority of our total caseload. HHC also treats more women, generally IV drug abusers, and children, the vast majority of whom are born to women who are IV drug users or mates of IV drug users. Thus, the typical AIDS patient seen at our facilities is indigent, has poor underlying health status, is an intravenous drug user with few community resources to fall back on for assistance and no health insurance or savings. While sixty (60) percent of them are Medicaid recipients or pending Medicaid eligibility, over twenty (20) percent are self-pay. Medicare accounts for only 1.5 percent of the payor class.

At this time we are not able to determine the precise costs of treating AIDS patients. However, we are developing a sophisticated cost accounting system that will enable us to capture detailed costs at the individual patient level. Preliminary estimates indicate that the average daily cost of treating AIDS patients is between $784 and $850, or approximately 60-70 percent more than the average daily cost of care for other medical/surgical patients.

We are projecting that we will spend in excess of $54 million on providing inpatient care to AIDS victims this fiscal year, less than half of which will be recaptured through third party reimbursement. Clearly, these costs are significant and not adequately reimbursed. The situation will only worsen as we move toward prospective payment reimbursement systems.

As you know, under the current DRG-based Medicare Prospective Payment System (PPS), we will be paid a flat rate per discharge, regardless of the actual cost, length of stay or intensity of care provided to the patient. Although Medicare represents only a small portion of our AIDS patient payor mix, Medicaid may well fall under a per case prospective payment system by 1987. This will cause serious problems for HHC and other hospitals treating large numbers of AIDS patients.

The Corporation has been involved in a number of special programs for AIDS patients. As early as 1983, HHC developed a corporate-wide employee training and patient education program; established an interdisciplinary group to review issues related to AIDS; initiated a resource utilization study to examine resource needs; instituted a weekly reporting and monitoring system; and entered into a contract to provide training for housestaff on the social problems of AIDS patients.

In March of this year, the Mayor announced a comprehensive expansion of existing City services for persons with AIDS. For HHC, this program meant the funding and expansion of a number of new initiatives including the following:

- The creation of ten interdisciplinary health care teams comprised of an infectious disease specialist, a nurse clinican and a social worker at eight HHC hospitals.

  These teams will provide routine and special medical and psychiatric consultation for all inpatients. When the patient is ready for discharge they will coordinate case management with primary providers in outpatient settings or smooth the transition into home care or other long term care placement. The team will be the focal point for implementing the tracking of all AIDS patients served by the facility, and will work with medical staff on treatment protocols and with other interdisciplinary staff on post-hospitalization psychosocial support needs.

- A new community-based ambulatory care clinic has been opened at the Community Health Project (CHP) at 208 West 13th Street in Manhattan. The clinic is the first ambulatory care clinic for persons with AIDS and the "worried well", and is a satellite to the AIDS program at Bellevue Hospital.

- An additional ten (10) bed adult AIDS unit at Bellevue Hospital is dedicated to the care of AIDS patients. This unit serves as the inpatient base for Bellevue's interdisciplinary team and also serves off-unit AIDS patients who are not in need of more intensive care.

- At Coler Hospital, a specialized AIDS long term care assessment team and ten long term care beds have been created. The assessment team consists of an infectious disease specialist, a psychiatrist, a nurse clinician and a social worker. The team evaluates all AIDS patients in HHC's acute care facilities who are ready for placement, so that an appropriate level of long term care can be selected and secured in an HHC facility, an HHC home care program or through programs provided by other agencies when the patient is ready for discharge. The beds with enriched staffing will be available for AIDS patients discharged from HHC acute care facilities who need long term care services involving intensive nursing and medical care.

- The City is currently working with the Archdiocese of New York to establish a shelter facility for homeless AIDS patients or patients in need of transitional supportive care following an episode of hospitalization. The Archdiocese has agreed to set aside a certain number of beds for people referred by the City.

- Another project that is in the planning stages is the development of a pediatric day care resource center for children with AIDS. About 50 percent of pediatric AIDS cases identified nationally exist in the New York Metropolitan area. The center will be located at the Bronx Municipal Hospital Center and will accomodate 25 children between the ages of three months to seven years. Staffing will include a pediatrician, nurse clinician, social worker, psychologist, physical therapist and an educator. Access to a dentist will also be provided.

Thus, while the City of New York continues to accelerate its funding and to expand its medical, social service and educational programs on behalf of those with AIDS, a significant commitment of federal resources has yet to be made. Clearly, Federal participation must be expanded.

- More funds must be allocated to research the cause of AIDS and to find a cure. The current budget request does not contemplate the allocation of new monies for AIDS research but instead relies on reprogramming funds previously designated for other medical research programs. The Mayor has decried this as a form of budgetary triage that pits one disease against another in the battle for research dollars.

- Currently AIDS patients are not eligible for Medicare unless they have been categorized and certified as disabled for a two year period. One half of the patients, however, die within the first two years of diagnosis. During this period these patients are usually severely disabled, have exhausted their financial resources, lost their homes, and needed intensive medical care and social services. AIDS patients deserve adequate care during this tragic time and Medicare eligibility should be established at the time of diagnosis.

- There are additional problems with Medicare reimbursement of AIDS. The Health Care Financing Administration must closely examine the DRG system as it relates to AIDS, and more accurately define a DRG for this disease. As DRGs are presently constituted, cases positively identified with an AIDS diagnosis fall into DRGs 398 (Immunity Disorders, Age Over 69 and/or complication) and DRG 399 (Immunity Disorders, Age Under 70 without complications). The resource intensity weights of these DRGs are .9753 and .7247 respectively.

  Resource intensity weights reflect hospital resources necessary to treat the average patient in a given DRG. Overall, resource intensity weights are set at 1.0 for the average patients. Thus average resources required by patients in DRGs 398 and 399 are less than those required by the average hospital patient. The average length of stay for DRG 398 and 399 patients nationwide is 8.1 and 6.4 days respectively, while HHC AIDS patients frequently stay as much as 50 days.

  Because of the low weights of these DRGs, any relief that might otherwise be gained by a case extending into outlier status will be proportionately low. A case can only be designated a cost outlier if it is not a day outlier. The day outlier thresholds for these DRGs are 23 and 21 days respectively. Thus, most HHC AIDS cases would receive day outlier payments (60% of DRG-specific per diem) and therefore not qualify for cost outlier payments (60% of the difference between actual costs, calculated at 72% of billed changes, and the DRG payment, or $13,000 regionally adjusted, whichever is lower).

The second major problem in DRG classification for AIDS cases occurs when the principal diagnosis (reason for admission) is one of the opportunistic infections occasioned by AIDS. Most frequent among these is pneumocystis carinii and Kaposi's sarcoma. These are assigned to DRGs 79, 80 and 81 for pneumocystis carinii and DRGs 283 and 284 for Kaposi's sarcoma. The same problems pertain, with variations, for these cases.

A broader strategy of federal support for long term care especially in catastrophic illness situations must be developed. There is a great and growing need for long term care services to meet the needs of AIDS patients who no longer require acute care in the hospital setting, but need continuing care and support in the home or in a structured residential health care setting. The City of New York has been a pioneer in developing comprehensive home care for all patients and institutional long term care services specifically for AIDS patients. While Medicaid, and to a much lesser extent, Medicare and private insurance, can be used to cover some of these services for eligible patients, there are important programmatic limitations and gaps in coverage which must be addressed. Medicare coverage for skilled nursing facility care and home health care is largely restricted to short term, post-acute care for the elderly. This is insufficient to meet the chronic longer term care needs of the younger AIDS patients. Currently, Medicare does not provide for chronic care in the home; homemaker/personal care services are not covered, and home health aide coverage is too limited in terms of hours and duration of service to assure the amount of care necessary to serve the AIDS patient. There is a need to provide an integrated and coordinated service plan at home which combines skilled care including nursing, therapies and home health aides, and personal care/support services.

- The Medicare hospice program should be adapted for AIDS patients by easing current eligibility restrictions and by raising the reimbursement ceiling, which is too low to assure the amount of service needed by AIDS patients.

- We strongly support the use of waivers such as those provided under the Section 2176 Home and Community-Based Services legislation. These waivers would allow states to amend their state Medicaid plans to include coverage for certain community services for defined populations as long as the cost of the service package does not exceed 100 percent of the equivalent costs for care in an institution. The Katie Beckett case provides another program model. If we could use such a waiver, which allows for services at home to certain eligible children without exhausting the financial resources of the family, we could assure services to children with AIDS.

In closing, I would like to stress that AIDS is a national problem. The Federal Government must demonstrate a leadership role and develop a comprehensive and coherent strategy for dealing with this major public health care crisis. Local governments must be relieved of bearing the entire burden of funding AIDS-related programs. HHC and the City of New York will continue to lobby for increased funding for health care, social services and housing for persons with AIDS as well as for disease surveillance, public health education and documentation of AIDS related discrimination. We will continue to assist you in developing alternative approaches to the problem of financing the delivery of medical services to AIDS patients.

Thank you again for the opportunity to present the views of the New York City Health and Hospitals Corporation on this critical public health care issue.

STATEMENT OF DR. ALFRED J. KATZ

Good morning, Mr. Chairman and members of the Committee. I am Dr. Alfred J. Katz, Vice President for Research, Development and Marketing of the American Red Cross. Thank you for this opportunity to testify concerning the impact that transfusion-associated AIDS has had on the nation's blood supply, and to offer an opinion regarding the research still needed if we are to be totally effective in the eradication and management of any possibility of transmission of AIDS by blood transfusion.

The American Red Cross is a nonprofit, nonsectarian, non-political organization chartered by the U. S. Congress to provide a variety of health and emergency support-related services. In this capacity, Red Cross annually collects more than six million units of blood from four million volunteer donors, and provides more than half of the blood and blood components transfused in the United States. Our responsibility is two-fold: to ensure the adequacy of the nation's blood supply, and to provide blood products that are as safe as possible. The recent emergence of AIDS compromised our ability to ensure the latter.

As of September 13, 1985, 225 instances of transfusion-associated AIDS, plus an additional 98 cases among hemophiliacs, had been reported to the Centers for Disease Control. Although these 323 patients represent barely 2.5% of all reported AIDS cases, transfusion-transmitted infections account for 20% of AIDS in childhood, and 10% of the AIDS in women.

Transfusion-associated AIDS, perhaps because of its occurrence in infants, perhaps because of the vulnerability of any of us, has received high media visibility. There is widespread understanding that AIDS may be transmitted by blood transfusion, which has resulted in considerable public anxiety. This knowledge has led a small number of people to defer surgery, or otherwise avoid medically necessary transfusions.

Fear of AIDS from transfusion has led some prospective blood recipients to recruit donors from among friends and family, and to avoid the community volunteer donor supply.

Anxiety about AIDS has also extended to the process of blood donation. The frequent association of AIDS with transfusion has created the impression that the disease can be acquired by blood donors. In a survey conducted last year by the American Association of Blood Banks, 43% of the adult Americans interviewed stated their belief that AIDS could be transmitted via the blood collection needle. This is a totally incorrect belief, but it probably has had negative impact on the ability of the blood collecting organizations in the United States to provide an adequate blood supply. Donor recruitment staff in many regions report increased difficulty in meeting collection goals, and there clearly have been intermittent shortages.

Under these circumstances, how have the blood collecting and transfusing agencies responded? Before the cause of AIDS was known, blood donor selection criteria were changed in 1983 to exclude those at high risk of AIDS, based on the presumption that AIDS was infectious.

Recent scientific advance has been of benefit of the hemophiliacs who depend upon coagulation factor concentrates prepared from pooled plasma. Most of the patients who received this material between 1980 and 1984 have evidence of exposure to the AIDS virus. However, it recently became apparent that HTLV-III can be neutralized by short exposure to heat. Today, all factor concentrates used in routine hemophilia care are heated, and we believe that for newly diagnosed, or previously untreated hemophiliacs, the danger of acquiring AIDS has been largely eliminated.

By far the most important, most effective response has been the implementation of a test for antibody to HTLV-III - a remarkable achievement made possible in large part by Federal funds provided to Dr. Gallo and his associates at the National Cancer Institute of NIH.

The availability of the HTLV-III antibody test has greatly improved our ability to screen for, and eliminate potentially infectious blood donors. There is clear evidence that the screening test now in use, when confirmed by a more specific technique, does identify individuals whose blood contains the AIDS virus. We estimate that Red Cross will identify 1600 potentially infectious, but otherwise apparently healthy such individuals this year.

Despite the deferral of high risk donors since early 1983, and the introduction of donor testing in 1985, it may be several years before we see a significant decrease in transfusion-associated AIDS among blood recipients. The disease will continue to occur, in some patients transfused and exposed to AIDS before 1983, in whom the disease has been latent.

All in all, Mr. Chairman, the blood supply for the American people has been maintained, and has been rendered virtually free of AIDS. What, then, remains to be done?

First of all, it is imperative that an even more sensitive screening test be developed for whole blood and its components. While measurement of an antibody response to HTLV-III is a major step toward making the blood supply safer, it has both theoretical and practical defects. It is essential that we develop a test that directly identifies infective blood, and this must be more sensitive, and more specific that the tests yet implemented. Moreover, we must be sure that it can detect intracellular virus so that transmission by leukocytes can be prevented for individuals who may not have free virus in the serum. This is a difficult and challenging task. Unless this assay can be carried out with instrumentation already available in blood banks, there will also be the engineering task of developing, testing and establishing this technology in blood banks throughout the country. We also are in need of confirmatory tests which are objective, specific, and rapid.

The long incubation period of HTLV-III means that we will not be absolutely certain that a test is satisfactory for several years after it is introduced. For this reason, all plasma products are being heat-treated in spite of the fact that the donors are all screened -- and found to be negative -- for anti-HTLV-III. Similarly, we must develop ways to inactivate viruses in whole blood and in blood components, including cryoprecipitate, platelets, leukocytes, and separated red cells, and develop even more effective methods for the treatment of plasma derivatives.

We are also concerned that studies be conducted to further understand the risk to patients who have been exposed to potentially infectious blood, and to understand the implications of the presence of anti-HTLV-III in an otherwise apparently healthy blood donor.

While these questions are paramount to those involved in blood transfusion, we also recognize the need to pursue both a vaccine and effective therapy.

Who should carry out this research? Many institutions must be involved. The difficult tasks of developing better assay methods and inactivating viruses require basic science as well as directed efforts and should be supported by the Congress. This research needs to be facilitated in universities, in the intramural programs of NIH and the CDC, in research institutes, and in industrial laboratories. There is no one group that should have the sole responsibility for AIDS research.

Mr. Richard F. Schubert, the President of the American Red Cross, has recently written to members of this committee in support of Secretary Heckler's request for a budget amendment for increased funding for AIDS research. Included in the proposed activities for additional funding are the studies that I have mentioned here, and we therefore continue to support the request.

Mr. Chairman, thank you very much for holding this hearing on the important issue of AIDS research. Progress has been made toward ensuring a blood supply free of the AIDS virus, but better diagnostic tests are needed, as are the means for evaluating the long-term prognosis of infected blood donors. It seems unnecessary to say that it will take enormous energy, funding, and luck for us to quickly develop effective therapy and a useful vaccine.

There is also a great need for education about AIDS, its transmission, prevention and containment - in order to clarify the non-relationship between AIDS and blood donation and thus create a positive impact on American attitudes toward blood donation. The American Red Cross, in fact, is planning a public education program.

The American Red Cross appreciates the opportunity to appear today, and we look forward to working with you and your staff in any way you consider would be helpful.

Dr. LEICHT. Thank you, Mr. Chairman.

As you mentioned, my name is Dr. Daniel Leicht, vice president for medical and professional affairs for the New York City Health and Hospital Corp. I am pleased to be here to participate in this hearing to emphasize an area completely not represented, that is areas of direct service to AIDS patients.

As you may know, over 35 percent of all reported AIDS cases are in New York City and over one-half of those receive services from the municipal sector. Figures from the last reporting period show 4,531 cases to date in New York City out of a total of 13,062 nationwide. In addition, 50 percent of all children with AIDS are in New York City. In New York City, AIDS has become the leading cause of death among men in their twenties and thirties and second highest cause of death among women between the ages of 30 and 34.

Since AIDS was first recognized nationally by the Centers for Disease Control in 1981, the city of New York has steadily augmented its funding for the enhancement of programs serving those afflicted with AIDS. These programs are aimed at educating the public about the disease, providing appropriate medical and social services and conducting epidemiological investigations and surveillance activities.

I represent the New York City Health and Hospitals Corp., the largest municipal hospital in the country. HHC plays a crucial role in addressing the special health care needs of the AIDS population since almost 40 percent of all AIDS beds in the city of New York are in HHC facilities. Our hospitals guarantee to all patients the right to quality health care in an atmosphere of human dignity regardless of ability to pay. The AIDS epidemic has placed a tremendous burden on our human, economic, medical, and technological resources. This burden can only be expected to increase as the incidence of AIDS continues its dramatic rise.

In spite of the alarming increase in cases, growing public concern and encouraging scientific discoveries, no comprehensive and coherent Federal strategy on AIDS has emerged.

Over 400 AIDS patients were admitted to our 11 acute care facilities last month alone, a significant increase over prior months. Our average daily census for AIDS is roughly 250 patients corporatewide. Over 30 percent of Bellevue's medical beds are now occupied by AIDS patients or symptom-diagnosed AIDS patients.

I would like to focus on some of the direct service delivery issues that are specific to the corporation in treating AIDS patients.

The cost of caring for AIDS patients is extremely high. This is attributable to a number of factors: Successive administrations throughout the course of the illness. Long lengths of stay due to severe medical complications, more intensive nursing care, higher levels of pharmaceuticals and supplies often involving expensive and some experimental anticancer drugs and the need for more frequent use of specialized equipment including dialysis units, all of which must undergo special sterilization procedures before it can be reused.

HHC has a particularly costly case mix of AIDS patients. We are currently treating a disproportionate share of cases in the IV drug abusing community who usually are much more ill with complications. Over the years, these cases have grown to represent a majority of our total caseload. Almost a reversal of the proportions of the national average. HHC also treats more women, generally IV drug abusers, and children, the vast majority of whom are born to women who are themselves or are the mates of IV drug users. Thus, the typical AIDS patient seen at our facilities is indigent, has poor underlying health status, is an intravenous—and has no health insurance or savings. While 60 percent of them are Medicaid recipients or pending Medicaid eligibility, over 20 percent are self-pay or have no means of payment. Medicare accounts for only 1.5 percent of the payor class.

At this time, we are not able to determine the precise costs of treating AIDS patients. However, we are developing a sophisticated cost accounting system that will enable us within the next year to capture detailed costs at the individual patient level. Preliminary estimates indicate that the average daily cost of treating AIDS patients is between $794 to $850. Approximately 60 to 70 percent more than the average daily cost of care for other medical patients.

We are projecting we will spend in excess of $54 million on providing inpatient care to AIDS victims this fiscal year, much less than one-half of which will be recaptured through third party reimbursement. Clearly these costs are significant and not adequately reimbursed. The situation will only worsen as we move toward prospective systems.

As you know, under the current DRG based Medicare prospective payment system, we will be paid a flat rate per discharge regardless of the actual cost, lengths of stay or intensity of care provided to the patient. Although Medicare represents only a small portion of AIDS patient payor mix, Medicaid may well fall under a per case prospective payment system by 1987.

The corporation has been involved in a number of special programs for AIDS patients. As early as 1983, HHC developed a corporatewide employee training and patient education program, established an interdisciplinary group to review issues, initiated resource utilization study and instituted a weekly reporting and monitoring system; and entered into a contract to provide training for house staff on the social problems of AIDS patients.

In March of this year, the mayor announced a comprehensive expansion of existing city services for persons with AIDS. For HHC, this program meant funding an expansion of a number of new initiatives. The creation of interdisciplinary health care teams comprised of infectious disease specialist, a nurse clinician and social worker.

These teams will provide routine and special medical and psychiatric consultation for all inpatients. When the patient is ready for discharge they will coordinate case management with primary providers in outpatient settings or smooth the transition into home care or other long-term care placement. The team will be the focal point for implementing the tracking of all AIDS patients served by the facility, and will work with medical staff on treatment protocols and with other interdisciplinary staff on posthospitalization psychosocial support needs.

A new community-based ambulatory care clinic has been opened at the community health project serving residents of New York on 13th Street in Manhattan. The clinic is the first ambulatory care clinic for persons with AIDS and the worried well, and is a satellite to the AIDS program at Bellevue Hospital.

An additional 10-bed adult AIDS unit at Bellevue Hospital is dedicated to the care of AIDS patients. This unit serves as the inpatient base for Bellevue's interdisciplinary team and also serves off-unit AIDS patients who are not in need of more intensive care.

At Coler Hospital, a specialized AIDS long-term care assessment team and 10 long-term care beds have been created. To our knowledge, this is one of the first in the country. The assessment team consists of an infectious disease specialist, a psychiatrist, a nurse clinician, and a social worker. The team evaluates all AIDS patients in HHC's acute care facilities who are ready for placement, so that an appropriate level of long-term care can be selected and secured in an HHC facility, an HHC home care program or through programs provided by other agencies. The beds with enriched staffing will be available for AIDS patients discharged from HHC acute care facilities who need long-term care services.

The city is currently working with the Archdiocese of New York to establish a shelter facility for homeless AIDS patients or patients in need of transitional supportive care following an episode of hospitalization. The Archdiocese has agreed to set aside a certain number of beds for people referred by the city.

Another project that is in the planning stages is the development of a pediatric day care resource center for children with AIDS. About 50 percent of pediatric AIDS cases, as I mentioned, identified nationally exist in the New York metropolitan area. The center will be located at the Bronx Municipal Hospital Center and will accommodate 25 children between the ages of 3 months to 7 years. Staffing will include a pediatrician, nurse clinician, social worker, psychologist, physical therapist, and an educator. Access to a dentist will also be provided.

Thus, while the city of New York continues to accelerate its funding and to expand its medical, social service, and educational programs on behalf of those with AIDS, a significant commitment of Federal resources has yet to be made. Clearly, Federal participation must be expanded. I will not speak to expand support for research as I am sure this has been well addressed today.

Currently AIDS patients are not eligible for Medicare unless they have been categorized and certified as disabled for a 2-year period. One-half of the patients, however, die within the first 2 years of diagnosis and few, if ever, return to employment after diagnosis or hospitalization. A recent survey of health workers at New York City hospitals who come down with AIDS shows that of 16 identified, 14 did not return to work and 2 returned for a very short period of time.

During this period these patients are either severely disabled, have exhausted their financial resources, lost their homes, and needed intensive medical care and social services. AIDS patients deserve adequate care during this tragic time and Medicare eligibility should be established at the time of diagnosis.

There are additional problems with Medicare reimbursement of AIDS and with Medicaid as with New York and other States move to payor systems. As I mentioned the DRG's with AIDS fall into 398 and 399 are very general categories, called immunity disorders. The waiving of those categories falls below the average DRG categories. In no way does this speak to the amount of resources that AIDS requires.

The average length of stay for these two DRG's are 8.1 and 6.4 respectively, while HHC AIDS patients frequently stay as much as 50 days.

Because of the low weights of these DRG's, any relief that might otherwise be gained by a case extending into outlier status will be proportionately low.

Senator Weicker. I want to get to that, Senator D'Amato had to excuse himself. He has another hearing. I do also. I want to make sure we get some questions in here and get the full testimony. I gather when you say there doesn't seem to be any concerted Federal policy, what you are talking about now is not the research effort as much as it is the taking care of patients.

Dr. Leicht. Looking at the impact——

Senator Weicker. Providing, in other words, with hospital beds and with care, is that not correct?

Dr. Leicht. Exactly.

Senator Weicker. I would certainly hope, because I agree with you, obviously coming from Connecticut, I have a chance to see my television, observe what is going on in New York. It seems to me there, indeed everywhere, nobody wants to provide shelter and care for these individuals. I am asking the same question. I am glad you are here to talk. I would like to know what is going on here, what are we going to do. We have these people. As I said in my opening remarks, we are not going to cast them like lepers in the sea or isolate them in a dungeon.

All the focus of these hearings is to prevent panic in the first place. Now we get to this very basic question, what are we going to do with the people who have it now? We are a civilized society and I don't think we are acting in a very civilized way at this juncture.

Dr. LEICHT. I agree with you totally. I think one of the greatest concerns most of the data we have about AIDS patients comes from hospitals. This is the reporting mechanism to the local health departments. We have very little information about the needs of patients, outpatients. Many of our patients are in the hospitals and don't need to be there. But because of support of home care or other alternative forms of care, we are supporting these patients in extremely expensive resource surroundings. As I mentioned 30 to 40 percent of medical beds at Bellevue are taken up by AIDS patients. Many of them do not need to be there.

Senator WEICKER. This is obviously a large part of the problem. I am not so sure we are addressing it correctly. We hope you will also afford a little more of your time to my staff. I don't know what we have got there in the budget package for this problem area. I am not sure we have anything.

A VOICE FROM THE FLOOR. Senator, could I say one word, please?

Senator WEICKER. I just think you better do something. Obviously we are going to have some sort of massive effort. I would like to get started on it.

What would you like to see not only as the first step in this area of the problem take place?

Dr. LEICHT. As I mentioned almost by definition, by the time of diagnosis and usually diagnosis occurs with the first complication, like hemolysis, like you heard from some of the researchers, at that point it is a disabling disease. Those individuals almost never return to work. Some form of expedited Medicare coverage would be a very significant step and Medicare that would address——

Senator WEICKER. What if the individual doesn't have any Medicare?

Dr. LEICHT. Doesn't have?

Senator WEICKER. What if it is one of those 35 million who don't have any Medicare coverage?

Dr. LEICHT. I am talking about Medicare eligibility on the basis of disability. These individuals——

Senator WEICKER. You are asking we extend the coverage?

Dr. LEICHT. That's right.

Senator WEICKER. Unfortunately, that is not within the purview of my committee.

Dr. LEICHT. I understand that but it is a Federal issue.

Senator WEICKER. I am glad you raise it. I will certainly forward your thoughts to the Finance Committee. I am wondering if there is anything this committee, Appropriations, can do now to assist?

Dr. LEICHT. I don't know about your authority——

Senator WEICKER. Is there any assistance from the Federal Government to those medical institutions that do make provision for AIDS patients, that is, such as the 10-bed project the mayor and the city of

New York have launched upon to be open this fall, could any portion of that be covered with Federal money?

Dr. LEICHT. I would think models like that that look at alternative—I think in particular we need assistance with support of alternative models of the care of AIDS patients. Again, I don't know the authority of your committee in terms of its funding——

Senator WEICKER. You have given me an idea. Maybe the point you make, maybe we need some pilot programs here in care. Maybe there is some way we can provide——

Dr. LEICHT. I think a large amount of care in New York City is provided on a volunteer basis.

Senator WEICKER. I think you are right.

Dr. LEICHT. Which I think has been heroic. That is getting stressed.

Senator WEICKER. As much as I admire and respect the Catholic Church, it is really a commentary on our Government that the Catholic Church has to step in with a program. I wish them all the best in the world, including success—that is not the problem of the Catholic Church. It is the problem of the Government which doesn't mean to say I don't think the Catholic Church shouldn't do it. It certainly is something—everybody is sitting around hoping somebody else will pick up the ball and run with it in this area. Is there any other main point you would like to make, Dr. Leicht. I would like to proceed with Dr. Katz.

I only have a few minutes. I will be glad to accept any other testimony for the record.

Dr. LEICHT. No; I think it is well expressed.

A VOICE FROM THE FLOOR. Mr. Chairman, may I have 1 minute?

Senator WEICKER. The witnesses are in the process of testifying. You, like I, have to listen and I think that is the best thing. I will now proceed with Dr. Katz.

STATEMENT OF DR. ALFRED KATZ

Dr. KATZ. I thank you very much for the opportunity to testify concerning the impact of AIDS in the transfusion of blood and offer an opinion of research still needed in this area.

The American Red Cross is an organization chartered by the U.S. Congress to provide health emergency services. In this capacity, we collected more than 6 million units of blood from more than 4 million individuals each year and more than one-half the blood is used throughout the country so our responsibility in this area is twofold, to ensure the adequacy of the blood supply and ensure the safety of that blood supply.

Recent emergence of AIDS compromised our ability in the latter area. As of September 1985, there were 225 cases of transfusion-associated AIDS plus an additional almost 100 cases among hemophiliacs. These total cases represent 2½ percent of all reported cases of AIDS, but almost 20 percent of AIDS in children and 10 percent of AIDS in women.

Because of its occurrence in infants and because of the vulnerability of all of us, transfusion-associated AIDS has received very high media visibility. There is a lot of understanding among the public that AIDS may be transmitted through blood transfusion. This knowledge has led a small number of people to defer surgery or otherwise avoid transfusion where it was, in fact, medically necessary. It has led people to select their own blood donors from among friends and family and finally it has led some people to avoid blood donation. This is an understandable confusion but totally incorrect to believe that AIDS might be contracted from the fact of donating blood.

Donor recruitment staff in many regions of the country report increased difficulty in meeting collection goals and there clearly have been intermittent shortages of blood throughout the country because of this concern.

Senator WEICKER. Is the concern one more of giving blood or is the concern that you are going to be screened in that process and if the screening would turn up a positive result and, therefore, you would be stigmatized? Isn't that the concern?

Dr. KATZ. No; I think most of the concern the donation that occurred 2 years ago, the last 2 years where there was not a screening test. Donors are informed that blood will be tested. If they don't want to be tested we ask that they not donate at all.

Senator WEICKER. Does this test take place after the blood has been given or before the donor gives?

Dr. KATZ. It takes place after the blood has been given.

Senator WEICKER. After?

Dr. KATZ. That is right. The donor is notified the test will take place before the donation is given.

Senator WEICKER. OK. Then to follow up on Senator D'Amato's question, he is notified the test will take place, the blood is taken, then the blood is tested?

Dr. KATZ. Correct.

Senator WEICKER. Is that donor ever notified about the result of that test?

Dr. KATZ. Most certainly. We think it is ethically imperative. We think it is medically very important we notified people who are indeed positive for the antibody. We are very careful though to do a confirmatory test on a positive initial screening test before we notify anybody. So that the people we notify have both a positive screening test and positive confirmatory test and they are told they have, in fact, been infected by the AIDS virus and that they may be infectious to somebody else. There are parts of the country where that kind of communication has not been possible because of local regulations, but those numbers of places are rapidly decreasing.

Senator WEICKER. Is all blood in the United States today, all blood screened?

Dr. KATZ. I believe——

Senator WEICKER. I am talking about by legitimate agencies?

Dr. KATZ. Yes; it is not yet mandatory but everyone is doing it.

Senator WEICKER. I am sorry, go ahead.

Dr. KATZ. That response to this AIDS emergency, the implementation of the testing by far has been the singlemost important thing that has happened, most effective thing we have done. The plasma that is used for treating hemophilia is now heat treated so that is no longer infectious.

Senator WEICKER. That is very important, isn't it. I think there is a good example as to—at the present time, in other words, the clotting factor, that is what it is known as.

Dr. KATZ. Right.

Senator WEICKER. Two years ago we couldn't guarantee anything. Now there is—what is the percentage of making that safe, almost 100 percent.

Dr. KATZ. Two years ago we could guarantee almost all hemophiliacs would be infected through the clotting factors and today we can say virtually no hemophiliac is affected through the clotting factor.

Senator WEICKER. What can you say as far as the blood plasma insofar as it is concerned, is that 100 percent safe now because of these screening procedures?

Dr. KATZ. Not 100 percent, but very close to it. Dr. Haseltine earlier pointed out the fact there are some very few people who have just been exposed to the virus and have not yet developed the antibody or may never develop the antibody. Current information suggests that that may be as little as 1 percent of the people who have been infected so that we think we have a test that is picking up 99 percent of the potentially infectious. That may leave us within this country with right now, maybe 30 units of blood a year out of 12 million units that are collected that may still be infectious. We don't have information——

Senator WEICKER. So we put this in a perspective, wouldn't that also be true of some other, excuse the unscientific term, bug in our blood that isn't AIDS, in other words? When we receive blood, isn't there some other factor?

Dr. KATZ. There are unfortunately other diseases that can be transmitted by blood. This degree of risk I just described is very, very safe. It is safer than what we have for some of these other conditions.

Given that degree of success in providing safe blood supply, what is there left to do? Well, I think we do need to pick up this additional 1 percent, whatever that number might be. We need a test that will identify not presence of the antibody but, in fact, the presence of virus so that we can, in fact, detect all the units that are potentially infectious. We need to have a confirmatory test which is objective, specific, and rapid. We need to be able to treat not only plasma, clotting factors but also whole blood and other blood components to eliminate any virus contamination that happens to be there, not only AIDS, but hepatitis as well.

We are also concerned that studies be conducted and some of these have been described earlier today, to follow up on the patients that have been exposed in the past years before we could test to find out what the implication is for them and we also need studies to follow the positive donors, people who come into our blood banks today apparently healthy but who test positive for the antibody to know what the long-term implication of this positive test is for them as well.

These are the questions that are paramount to those involved in blood transfusion but we certainly also recognize the need to pursue the vaccine and effective therapy that has been discussed earlier today as well. So with those remarks, Mr. Chairman, I would like to thank you for holding the hearing, for allowing me to testify on this subject and to offer any help to your committee in this process.

Senator WEICKER. Dr. Katz, thank you very much. Dr. Leicht, thank you. With this testimony in hand, these and the prior witnesses, the subcommittee will now proceed to the appropriations task with markup before the full committee being on next Tuesday. I would expect that there might be additional developments in regard to the money requested, and I would ask the staff of the various Senators who sit on the subcommittee to work with my staff and develop whatever additional figures are necessary or reshift whatever the priorities seem to be in the moneys already allocated by virtue of the subcommittee markup. Once that task is done and once the full committee markup takes place, we will again review the amounts supplied in the funding of AIDS prior to action on the floor.

Indeed if there are additional requests or additional testimony, once again the amounts will change prior to final action.

ADDITIONAL SUBMITTED STATEMENTS

The record will also remain open for any comments by members of the committee or any comments by the public.

[The statements follow:]

STATEMENT OF SENATOR ALAN CRANSTON

Mr. Chairman, I am pleased to have this opportunity to present testimony on the devastating AIDS epidemic. I would like to express my deep appreciation to you, Senator Weicker, as distinguished Chairman of this Subcommittee, for holding this hearing today on AIDS -- the first in the Senate -- to examine what steps need to be taken this year to help bring us closer to stopping the spread of this deadly disease and, ultimately, to eliminate it. I would also like to congratulate you for your steadfast support and leadership in ensuring that adequate resources are made available for fighting AIDS.

Research

During the first few years of the AIDS crisis, it was most critical to channel our efforts into basic research. Because of that effort, in less than four years scientists have identified the HTLV-III/LAV virus as the causative agent of AIDS, unraveled its many symptoms, and devised a blood screening test to safeguard the nation's blood supply. Years of basic research have produced a solid scientific foundation on which efforts to develop effective therapies to treat AIDS and a vaccine making it possible ultimately to eradicate AIDS can be developed.

Thus, at this point, rapid advances are being made in therapeutics and new compounds are becoming available that warrant thorough study of their potential for effectively treating AIDS. Many such drugs are reaching the point at which first and second stage clinical trials are possible, and many more are awaiting safety and efficacy testing.

As a result, there is a growing consensus within the scientific community that now is the time to make an accelerated effort to see that promising drugs are vigorously pursued and properly tested. However, the Administration's budget request -- even as modified by Health and Human Services Secretary, Margaret Heckler's July 19, 1985, submission, to add $9.7 million for research for vaccines and therapeutics -- does not allow for expanding and expediting efforts that are needed in order for us to develop as swiftly as reasonably possible the ability to treat and ultimately cure and prevent AIDS. Under the Administration's budget, many potentially beneficial therapies will go untested and many individuals with AIDS who desire to participate in clinical trials will be unable to do so. Hence, we would not be making the maximum effort to halt the spread of this killer disease.

In this connection, I would note that, because of the unavailability in the United States of many drugs undergoing clinical trials elsewhere, some Americans with AIDS have left the country for France or Mexico, away from the supportive environment of their families and friends, in order to participate in clinical trials or to obtain experimental drugs.

Based on the foregoing, I believe that additional funds should be included in the FY 86 Labor/HHS/Education Appropriations Act to implement a vigorous investigative effort for effective treatments. According to some of the most prominent AIDS researchers in the country, $70 million above the current budget request is needed for this effort. I further understand that NIH has under development a coordinated plan of new initiatives in AIDS research, particularly in the area of therapeutics, which would warrant such an investment in FY 86. The additional funding would enable scientists to search for and develop new drugs to inhibit the virus, to stimulate the immune system, and to treat "opportunistic" infections often associated with AIDS.

Development of effective drugs to inhibit the virus is an essential component to finding a cure for AIDS. Moreover, these drugs hold great promise in preventing individuals who have been infected with HTLV-III/LAV but have not developed AIDS or AIDS-related complex -- a less severe or pre-AIDS condition -- from developing symptoms or possibly transmitting the virus to other people. More than one million Americans may have already been infected and, while most may never develop AIDS, they may remain infectious for many years.

Now is the time, as part of an expanded AIDS research effort, to establish regional AIDS treatment evaluation units to test promising drugs on a wide range of patients -- those with a full range of AIDS symptoms and those with varying stages of AIDS related complex -- in order to gather scientific data, quickly and accurately, about their effectiveness. Ten such units throughout the country would be able to provide treatment to large numbers of individuals in or near the cities in which they live. In addition, these evaluation units would enable multi-center clinical trials of AIDS treatments to be coordinated and conducted in a uniform manner.

Researchers in my home state of California have repeatedly stated that state and local governments have supported the cost of basic and clinical research in their laboratories because federal funds were unavailable. With thousands of AIDS patients throughout the country, it is critical that the federal government provide leadership in battling AIDS by supporting and coordinating such research efforts.

The additional funding would also provide for the acceleration of efforts to improve medical diagnostic capabilities on AIDS. Although the antibody blood-screening test has nearly completely eliminated the threat of transmitting the virus through the blood supply, it is not useful as a diagnostic tool for AIDS or for detecting the presence of the virus in blood or blood components. Moreover, the procedures currently used to detect the virus or to confirm the presence of the antibody to the virus are costly and laborious.

Finally, I understand that the Public Health Service is considering a research program for the formulation, production, and distribution of so-called "compassionate drugs" for AIDS -- under which Investigational New Drug exemptions could be granted for selected non-FDA approved drugs when there are no other therapies to treat the disease. Such a program could help avert the recent situation regarding HPA-23, in which many Americans went to Paris to receive treatment because it was previously unavailable in the U.S. Some of the additional $70 million could also be used in connection with this new program.

Community education and risk reduction

Mr. Chairman, I am pleased that Secretary Heckler's July 19 budget submission, which your Subcommittee has approved, adding $40.7 million to the FY 1986 funding for AIDS activities, included $21.7 million for community health education and risk reduction for AIDS. Without a vaccine to the HTLV-III virus -- and the development of one appears to be years away -- prevention through such a program is our best hope for limiting the spread of infection. This $21.7 million would be invaluable to states, local communities, and community-based health organizations in their efforts to educate both the general public and members of high-risk groups about AIDS.

In this regard, I very much appreciated the help and support that you, Mr. Chairman, and Senator Proxmire, the ranking Democrat on the Subcommittee, and others provided in the development and adoption of report language in the June 13 report accompanying the FY 85 Supplemental Appropriations Act -- S. Rep. 99-82 requesting the Centers for Disease Control to develop a comprehensive education and risk reduction program. I would note that the program, as outlined in the budget request, is consistent with the Committee's directive.

Inappropriateness of Funding by Transfer

Mr. Chairman, I am also pleased that the Subcommittee rejected the Administration's proposal to expand efforts on AIDS by using funds originally intended for other programs -- the National Health Service Corps, the Indian Health Service, the CDC virology laboratory, and the National Institutes of Health.

As I noted in my September 13 letter to you, Mr. Chairman, which I have appended to my testimony, I opposed such a diversion of funds because it would disrupt many ongoing programs and would fail to recognize that the AIDS problem can only be solved by a coordinated, sustained effort which requires a long-term funding base -- not the repeated shuffling of funds at the last minute..

Conclusion

In conclusion, Mr. Chairman, I strongly urge that the Committee on Appropriations include in the Labor/HHS/Education Appropriations Act an additional $70 million, above the Administration's request, for the purposes of expanding clinical research efforts and developing a compassionate drug program.

LETTER FROM SENATOR ALAN CRANSTON

September 13, 1985

Honorable Lowell P. Weicker, Jr.
Chairman
Subcommittee on Labor, Health and Human
  Services, Education, and Related Agencies
Committee on Appropriations
United States Senate
Washington, D. C. 20510

Dear Lowell,

I'm writing to you in your capacity as Chairman of the Appropriations Subcommittee on Labor, HHS, Education, and Related Agencies and a steadfast supporter of research and other public health efforts to combat AIDS. I strongly urge that your Subcommittee include an adequate FY 1986 appropriations for AIDS activities, particularly research and public education -- specifically, the additional $40.7 million in FY 86 funding provided for in the July 19, 1985, budget request submitted by HHS Secretary Heckler as well as a $70 million increase primarily for AIDS treatment research and clinical trials.

Community education and risk reduction. -- I am pleased that a significant portion of the July 19 budget request -- $21.7 million -- is for community health education and risk reduction for AIDS. Without a vaccine to the HTLV-III virus -- and the development of one appears to be years away -- prevention through such a program is our best hope for limiting the spread of infection. This $21.7 million would be invaluable to states, local communities, and community-based health organizations in their efforts to educate both the general public and members of high-risk groups about AIDS.

In this regard, I very much appreciated the help and support that you, Senator Proxmire, the ranking Democrat on the Subcommittee, and others provided in the development and adoption of report language in the June 13 report accompanying the FY 85 Supplemental Appropriations Act (S. Rep. 99-82), requesting the Centers for Disease Control (CDC) to develop a comprehensive education and risk reduction program. I would note that the program, as outlined in the budget request, is consistent with the Committee's directive.

The July 19 budget request represents a good step toward developing a comprehensive program to deal with AIDS -- through enhanced epidemiological, research, and education efforts. However, I am very concerned that the resources needed for AIDS activities not be provided through the diversion of funding from other vital health programs. The Administration's budget request proposes to expand efforts on AIDS by using funds originally intended for other programs -- the National Health Service Corps, the Indian Health Service, the CDC virology laboratory, and the National Institutes of Health (construction grants).

With the new fiscal year beginning in less than a month, diverting funds from these programs, especially so late in the budget cycle, would disrupt the ability to provide needed health services and delay the upgrading of facilities critical for the progress of research. In light of previous reprogramming actions, the Office of Technology Assessment concluded in February 1985 that transferring funds from other activities in order to fund efforts on AIDS resulted in "inadequate planning, increased competitiveness among agencies, inadequate attention to certain areas which are perceived by many to be important ... and a diversion of attention from other critical health areas."

In addition, a transfer action fails to recognize that the AIDS problem will not be solved in the very near future. Rather, the epidemic will be halted only by scientists, public health officials, private industry and the public at large working together in a coordinated, sustained effort which requires a long-term funding base -- not the repeated shuffling of funds at the last minute.

Research. -- With regard to funding research, there is a growing consensus within the scientific community that now is the time to make an accelerated effort to see that promising drugs are vigorously pursued and properly tested. Although the Administration's new budget request adds $9.7 million for research for vaccines and therapeutics, the Administration's proposed funding level for research is such that many potentially beneficial therapies will go untested and many individuals with AIDS who desire to participate in clinical trials will be unable to do so. Because of the unavailability in the United States of many drugs undergoing clinical trials, some Americans with AIDS have left the country for France or Mexico, away from the supportive environment of their families and friends, in order to participate in clinical trials or to obtain experimental drugs.

Rapid advances are being made in therapeutics and new compounds are becoming available that warrant thorough study of their potential for effectively treating AIDS. Many such drugs are reaching the point at which first and second stage clinical trials are possible, and many more are awaiting safety and efficacy testing.

In addition, basic research is progressing rapidly, producing more definite results and numerous new leads. In the four years since this epidemic began, scientists have identified the causative agent of the disease, unraveled its many symptoms, and devised a blood screening test to safeguard the nation's blood supply. The research budget must be allowed to grow commensurate with the progress in the field in order to make possible the development of new leads and to find the means to end the epidemic as rapidly as possible.

Thus, I believe that additional funds should be included in the FY 86 Appropriations Act to implement a vigorous investigative effort for effective treatments. According to some of the most prominent AIDS researchers in the country, $70 million above the current budget request is needed for this effort. I further understand that NIH is developing a coordinated plan of new initiatives in AIDS research, particularly in the area of therapeutics, which would warrant such an investment in FY 86. The additional funding would enable scientists to search for and develop new drugs to inhibit the virus, to stimulate the immune system, and to treat "opportunistic" infections often associated with AIDS.

Finally, I understand that the National Cancer Institute is considering a research program for the formulation, production, and distribution of so-called "compassionate drugs" for AIDS -- under which Investigational New Drug exemptions could be granted for selected non-FDA approved drugs when there are no other therapies to treat the disease. Such a program could help avert the current situation regarding HPA-23, in which many Americans have gone to Paris to receive treatment because it was unavailable in the U.S.

* * * * *

Accordingly and in sum, I urge that that the Subcommittee include in the bill it reports an additional $40.7 million (not by way of transfer) for education, epidemiology and research on AIDS, and an additional $70 million, above the Administration's request, for the purposes of expanding clinical research efforts and developing a compassionate drug program at the National Cancer Institute.

Lowell, I am hopeful that we can work together on this urgent matter and I look forward to your response.

With warm regards,

Cordially,

Alan

Alan Cranston

STATEMENT OF SAMUEL B. WALLACE

My name is Samuel B. Wallace. Some years ago I discovered an effective treatment for respiratory illnesses using FDA approved antibiotics. I have every reason to believe that because this formula is so effective in treating a wide range of respiratory illnesses including pneumonia, influenza, asthma, the measles, the mumps, cholera, and meningitis that it would be effective in treating immunodeficient diseases such as leukemia and AIDS.

I have discussed my formula with FDA officials and they have assured me that this formula is very safe because it combines a nontoxic antibiotic with a solution that is 99 percent water. And because the antibiotic is also administered in 10 percent of normal dosages when it is applied nasally.

I have made great efforts to have my formula tested by the NIH. The latest test that I have proposed, informally, is a 1-day test against asthma and the reduction of viral and bacteria fevers because asthma can generally be cured in 1 days time and viral and bacterial fevers are reduced in 1 days time to near normal temperature levels.

The NIH has thus far refused to test my medical formula which I believe could be tested in a small pilot program against asthma and fevers in 1 days time in order to determine its basic effectiveness. They have offered a cumbersome grant proposal procedure that is so cumbersome that it would take 6 months for review and their suggestions of alternative ways for having my formula tested by the NIH ignored the fact that only limited data can be given to them other than my word that this formula has been tested and has been effective against all the diseases mentioned above and that in the case of meningitis that I personally had the disease which can cause paralysis on several occasions in Brazil and twice in this area and that my formula worked in treating myself and others against meningitis in Brazil. (I have requested information from the Brazilian Government that they may have access to thorough tests that some of their medical officials and personnel ran in 1972 and 1973. I have received no response to my request made last week to that request.)

The NIH's refusal thus far to test my formula of the antibiotic combined with phenylephrine HCl or naphazoline HCl is ironic when, in fact, the NIH has long promulgated a sister drug—adriamycin which in chemical compositionis similar to the antibiotic nose drops for which I have requested 1 day tests.

Adriamycin is composed of naphazoline HCl in solution with a derivative of streptomycin and is one of the most widely used anticancer drugs that both the NIH cancer specialists and American Cancer Society physicians use. However, adriamycin is according to Dr. Bonnana, the great cancer specialist of Italy-Cardio Toxic, in 10 percent of the time.

My formula composed of penicillin plus Neosynephrine HCl in 1 percent solution has been declared absolutely safe by FDA officials. I, therefore, request that in the interest of science and humanity and particularly for those suffering from immunodeficient diseases that the Senate Appropriations Committee pass a resolution requesting the NIH to run 1 day trials of this medical formula. And if those trials prove effective that it be tested against cancer and AIDS.

CONCLUSION OF HEARING

Senator WEICKER. With that the subcommittee will stand in recess.

[Whereupon at 2:13 p.m., Thursday, September 26, the hearing was concluded, and the subcommittee was recessed, to reconvene at the call of the Chair.]

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